American Journal of Diseases of Children

VOLUME 37 APRIL, 1929 NUMBER 4

SEDIMENTATION REACTION IN CHILDREN *

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During the past year, a study has been made of the sedimentation rate of the red blood cells in children, with a view of obtaining information which might be of practical clinical value. A study of the literature on the sedimentation reaction reveals a comparative scarcity of reports concerning pediatrics;[1] the majority of communications pertain to gynecology and obstetrics[2] and to tuberculosis.[3] The history of the development of the sedimentation reaction begins with observations made by Galen, Hewson, Hunter,[4] Biffi[5] and others. In 1897, Biernacki[6] proposed a method for determining the sedimentation reaction and reported clinical and experimental observations. Fahraeus[7] proposed another clinical method in 1918. Westergren[8] modified the procedure in 1920 and subsequently, Linzenmeier proposed a simplified procedure[9] and has added a micromethod.[10] Many other modifications of the technic and new methods have been offered,[11] all based on the same principle, namely, the time required for the erythrocytes to settle out of their plasma suspension. A number of theories have been proposed in explanation of the sedimentation reaction,[12] and considerable experimental work has been done.[13] Fahraeus[14] stated that the change in sedimentation is a physicochemical phenomenon dependent on a variation in the properties of the plasma; that is, a qualitative change in the serum globulin, principally fibrinogen. Since the globulin has a high agglutinative power and since the agglutinative capacity of protein is related to the colloidal state, it follows that the suspension stability of the cells is dependent on the colloidal state. The majority of investigators agree on this premise.[15] The fibrinogen content of the blood is increased in certain diseases[15a]—leukemia, pneumonia, pleurisy, rheumatic fever, erysipelas, suppurative infections, diphtheria, scarlatina, rubeola, typhoid fever, influenza, tuberculosis and syphilis. In these diseases, the rate is usually most rapid. The fibrinogen content of the blood is decreased

* Submitted for publication, Oct. 23, 1928.

* From the Milwaukee Children's Hospital.

* Read before the Section on Diseases of Children at the Seventy-Ninth Annual Session of the American Medical Association, Minneapolis, June 13, 1928.

in severe degenerative lesions of the liver, in the anemias, especially pernicious anemia, and in these conditions the rate is decreased.[4] The theory of the difference in electrical potential between the negatively charged red cells and the positively charged protein elements (fibrinogen) in the plasma proposed by Hober [16] and supported by a number of investigators [17] probably rests on the globulin content already outlined. While the size, hemoglobin content and other characteristics of the red cells are factors in the reaction,[18] the principle is dependent on changes in the plasma.

From the literature, one may conclude that the sedimentation rate has certain characteristics in the normal [19] with rather wide physiologic variations,[20] in relation to respiration,[21] blood pressure,[22] digestion [23] and thirst.[24] External influences such as heat,[25] baths [26] and radiation [27] exert considerable effect on the rate, as do the internal secretions [28] and certain drugs.[29] The rate is usually increased in acute inflammation and infection,[30] in infectious diseases [31] and in tuberculosis,[3] in which it is said to parallel the degree of activity of the lesion.[32] The rate is reported to be considerably increased in pneumonia,[33] in acute arthritis [34] and in malignant diseases.[35] Syphilis,[36] malaria,[37] leprosy [38] and Addison's disease [39] also cause an increase in the rate of sedimentation, while anemia, jaundice,[40] cirrhosis, cardiac stasis, liver metastases and gallstones may cause a retardation.[41] The rate may be normal in gastric ulcer, cardiovascular disease, lesions of the kidneys and exophthalmic goiter,[42] and increased or decreased in diseases of the blood.[43]

Studies have been made of the sedimentation of erythrocytes in nervous and mental diseases.[44] It is concluded [45] that the rate is increased in senile dementia, neurosyphilis, general paralysis, catatonia and in epilepsy immediately after an attack; there is no change in the constitutional psychopathies, neurasthenia, hysteria, manic-depressive insanity and paranoia. The sedimentation rate has been studied in the various special fields of medicine, in pediatrics,[1] gynecology and obstetrics [2] and in tuberculosis,[3] as already mentioned. It has also been studied in internal medicine,[46] surgery,[47] orthopedics,[48] urology [49] and dermatology,[50] as a special diagnostic aid. While the experience of a large number of investigators in an extensive series of cases [51] stimulates considerable enthusiasm over the value of sedimentation reaction as a clinical aid,[52] there are not a few conflicting reports.[53] Certain authors consider the test of limited value in distinguishing abnormal from normal,[54] and others consider it useless and of no value.[55] Most of the work on the sedimentation reaction in children appears in the German literature. With a technic of their own, Brokman and Hirzfeld [56] found a slow sedimentation rate in blood from the cord, one-sixth or one-seventh the rate of the mother. The fetal plasma showed the rate of the mother's erythrocytes. The rate was found increased in

tuberculosis, febrile conditions, diabetes mellitus, von Jaksch-Hayem's anemia, bronchiectasis, articular rheumatism and decomposition.

Langer and Schmidt,[57] also with a modified technic of their own, established a small series of normals and reported an increased rate in tuberculosis and pyogenic infections, a normal rate in intertriginous eczema and scrofulous eczema, and a "slowed" rate in exudative diathesis. Wail [58] used Pantschenkoff's micro-method and reported normal rates in the following conditions: progressive muscular atrophy, eczema, purpura, myatonia, pyloric stenosis, neuropathies, bronchial asthma, nanism, chorea minor, malaria and gigantism; moderately increased rates in hydrocephalus, osteopsathyrosis, acute bronchitis, typhoid, bronchial asthma, chronic arthritis, tuberculous bronchial adenitis, erythema nodosum and cerebrospinal meningitis; strongly increased rates in hepatic sarcoma, pyelocystitis, pericarditis, leukemia, chronic endocarditis, catarrhal pneumonia and in active tuberculosis,

TABLE 1.—*Normal Controls in Infants Aged from One to Eleven Months*

1 month	6 hours 30 minutes
3 months	2 hours 45 minutes to 1 hour 40 minutes
4 months	2 hours 35 minutes to 1 hour 15 minutes
5 months	2 hours 0 minutes to 1 hour 0 minutes
6 months	3 hours 10 minutes to 1 hour 30 minutes
7 months	3 hours 30 minutes to 2 hours 50 minutes
8 months	2 hours 0 minutes to 1 hour 50 minutes
9 months	2 hours 0 minutes to 1 hour 30 minutes
10 months	3 hours 10 minutes
11 months	2 hours 15 minutes

except tuberculous meningitis, in which the increase is only moderate. Wail [58] considered the reaction of value only in ruling out or indicating inflammatory processes.

Nadolny [59] found the sedimentation rate slow in infants, slowest at the age of 2 months. György [60] found the opposite. Duzar corroborated Nadolny's observations and associated the sedimentation rate with the globulin fraction. Torök studied eighteen new-born and eighty-three older infants and found the Gerloczy reaction positive in those conditions with reported increased sedimentation rates.

In 110 cases, Duzar and Rusznyak [61] studied the Daranyi, Gerloczy, and Frisch-Starlinger tests, and the Linzenmeier sedimentation rate, and estimated the protein fraction with a nephelometer. They considered the sedimentation rate to depend on the protein content. Hille [62] used the Linzenmeier technic with twenty-nine healthy infants. He concluded that the changes in the sedimentation rate depended on the state of dispersion of the plasma colloid or blood colloid liability and was influenced by the red cell count and hemoglobin and by digestion. The normal controls in infants, aged from 1 to 11 months, are given in time required to settle 18 mm. (table 1).

Lederer [63] made parallel studies on ninety-two well children, determining the serum protein content, lipase content and the sedimentation rate (Linzenmeier technic), reading the time required to clear 18 mm. The protein and lipase content of the serum increase with age as does the sedimentation rate. To the second year, the rate was from one to one and one-half hours; to the third to the fourth years, from one to two hours; fifth to sixth years, two hours faster; after the sixth year the rate was slower until the tenth year, when it approximated that of the adult. The rate was increased in the spring of the year.

Opitz and Frei,[64] using Plautschen's method, reported a markedly increased rate in syphilis and in acute inflammations, especially acute nephritis and pharyngitis, and a markedly decreased rate in tuberculous meningitis, chlorosis and congenital heart disease. Stern [65] studied sedimentation rates of twenty rachitic infants who were not anemic. The Westergren method was used, and determinations of phosphorus were made. The normal rate for an infant, aged 4 months, is given as high as: a half hour, 21 mm.; one hour, 34 mm.; two hours, 101 mm., and twenty-four hours, 203 mm. One reading for a rachitic infant, aged 4 months, is given as one-half hour, 5 mm.; one hour, 10 mm.; two hours, 50 mm., and twenty-four hours, 64 mm. There was always a marked delay of the rate in rachitis. Stern also demonstrated the influence of stasis.

Pflüger reported on 1,200 tests and stated that one determination was of no value. A series of tests was of value in determination of activity of a tuberculous process. Bardach [66] found a difference of 100 per cent in the rate on the same normal on different occasions. Trias [67] investigated the sedimentation rate in seventy-six children before and after making a Pirquet test. In children reacting positively to the tuberculin test, 65 per cent showed an increased rate after the test; 10 per cent showed a decreased rate, and 25 per cent were not influenced. Greisheimer and his associates [68] reported considerable variation in normals, not related to sex, age or meals.

In the interpretation of the sedimentation rate, two important factors have recently been emphasized which apply to almost all of the methods used. The character and amount of anticoagulant used and venous stasis both have considerable bearing on the result obtained. Rubin and Smith [69] repeated the earlier observation that any anticoagulant alters the quantitative relation between plasma and cells and so is unsuitable for a study of red cells. They made a comparative study of the sedimentation rate with citrate, potassium oxalate and hirudin as the anticoagulants and reported that the hemoglobin paralleled the sedimentation rate to a certain degree. The cell volume was closely related to the twenty-four hour sedimentation but not to the two hour reading. Anticoagulants cause a change in the osmotic pressure of the blood due

to a change in the size of the red cells. Sodium oxalate causes a shrinkage in cell volume, and the greater the cell volume the greater is the shrinkage. Plass and Rourke [70] demonstrated that venous stasis caused a decrease in plasma volume with an increased sedimentation reaction.

In our earlier studies we used the modified Linzenmeier method with a 1 cc. Luer Fournier syringe graduated in 0.01 cc. sections. This procedure did not allow of accurate determination, and the Westergren method was adopted. This method consists of drawing 1.2 cc. of venous blood, without stasis, into 0.3 cc. of 3.8 per cent sodium citrate solution, a dilution of 4:1. This diluted blood is drawn up 200 mm. in a capillary tube with a bore of 2.5 mm., and the tube is placed vertically in a rack. The column of clear plasma above the settling red cells is read in millimeters at one-half, one, two and twenty-four hours. In addition to this procedure, venous blood was mixed in one tube of

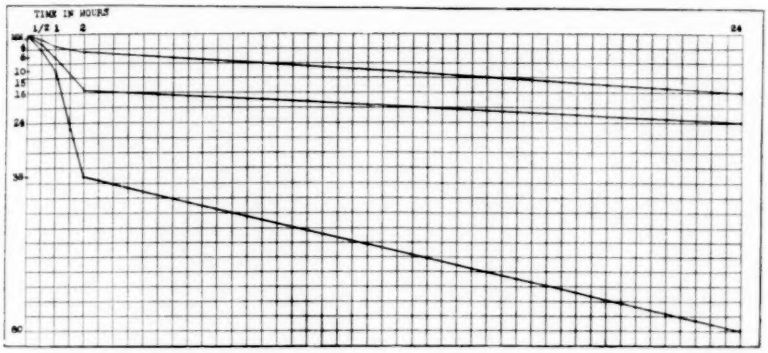

Chart 1.—Normal variations in children (citrate).

potassium oxalate powder and in another tube with heparin. Samples of blood with these two anticoagulants were then drawn into similar capillary tubes, and the three sedimentation rates were studied. Parallel hemoglobin determinations (Dare), erythrocyte, leukocyte and differential counts, Wassermann tests (Noguchi), and microprecipitation tests were made. Whenever there was sufficient blood the group was determined, and quantitative analyses of calcium, phosphorus, sugar, urea nitrogen and nonprotein nitrogen were made.

Our preliminary results (150 tests) with the modified Linzenmeier syringe method are not tabulated. For normal controls (table 2 and chart 1), we made determinations on thirty-one well, healthy children and five infants from orphanages on two different occasions (table 3). The blood was taken before breakfast, between 7:30 and 8:30 a. m. As normals, six healthy adults were also studied for daily variations in relation to meals and activity (table 4 and chart 2). Sedimentation rates were made with normal bloods after exposure to room temperature,

TABLE 2.—*Sedimentation Rate in Normal Children*

Name	Sex	Age, Yrs.	Readings in Mm.	Sedimentation in Hours ½	1	2	24	Hemoglobin, per Cent	Red Blood Cells	White Blood Cells	Differential: Polymorphonuclears	Small Lymphocytes	Large Lymphocytes	Large Mononuclears	Transitionals	Eosinophils	Plasma, per Cent by Volume 2 Hrs.	24 Hrs.	Date
S. B.	M	10	Citrate	0	1	6	54	..	...	.....	..	..	..	..	..	..	3	27	
			Oxalate	0	1	8	34	..	...	.....	..	..	..	..	..	..	4	17	
			Heparin	..	..	..	..	85	463	8,050	58	30	2	6	4	..	..	....	6/16/28
			Citrate	0	5	28	70	..	...	.....	..	..	..	..	..	..	14	35	
			Oxalate	0	10	12	33	..	...	.....	..	..	..	..	..	..	6	16.5	
			Heparin	..	..	..	..	81	451	8,600	62	21	8	4	3	2	..	....	7/11/28
E. W.	M	12	Citrate	0	0	10	71	..	...	.....	..	..	..	..	..	..	5	35.5	
			Oxalate	0	1	82	101	..	...	.....	..	..	..	..	..	..	41	50.5	
			Heparin	2	10	40	88	83	481	9,100	70	20	2	6	3	..	20	44	6/16/28
			Citrate	0	0	4	65	..	...	.....	..	..	..	..	..	..	2	32.5	
			Oxalate	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Heparin	..	..	..	..	81	472	9,300	69	18	4	5	4	..	..	.....	7/ 7/28
E. M.	M	9	Citrate	0	2	10	85	..	...	.....	..	..	..	..	..	..	5	42.5	
			Oxalate	1	4	15	60	..	...	.....	..	..	..	..	..	..	7.5	30	
			Heparin	3	12	46	80	81	468	9,340	57	35	4	2	2	..	23	40	6/16/28
Home C. C.	M	14	Citrate	0	5	15	84	..	...	.....	..	..	..	..	..	..	7.5	42	
			Oxalate	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Heparin	..	..	..	..	76	464	10,500	43	45	8	4	..	..	..	....	6/16/28
Home D. F.	M	13	Citrate	0	2	8	65	..	...	.....	..	..	..	..	..	..	4	32.5	
			Oxalate	1	5	20	45	..	...	.....	..	..	..	..	..	..	10	22.5	
			Heparin	0	5	25	70	83	464	8,100	48	38	8	4	2	..	12.5	35	6/16/28
Home G. B.	M	6	Citrate	0	3	22	55	..	...	.....	..	..	..	..	..	..	11	27.5	
			Oxalate	1	12	36	58	..	...	.....	..	..	..	..	..	..	18	29	
			Heparin	5	40	51	85	81	472	7,850	35	45	10	4	1	..	25.5	42.5	7/10/28
A. W.	M	7	Citrate	2	5	15	40	..	...	.....	..	..	..	..	..	..	7.5	20	
			Oxalate	3	15	14	65	..	...	.....	..	..	..	..	..	..	7	32.5	
			Heparin	..	..	..	..	89	471	10,050	37	45	13	3	2	..	..	....	4/21/28
			Citrate	0	10	62	83	..	...	.....	..	..	..	..	..	..	31	41.5	
			Oxalate	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Heparin	..	..	..	..	87	462	9,785	65	31	1	2	..	1	..	....	7/10/28
F. F.	M	11	Citrate	3	5	10	80	..	...	.....	..	..	..	..	..	..	5	40	
			Oxalate	2	10	25	40	..	...	.....	..	..	..	..	..	..	12.5	20	
			Heparin	2	20	54	78	82	454	9,350	35	37	23	5	..	..	27	39	4/21/28
			Citrate	0	0	10	92	..	...	.....	..	..	..	..	..	..	5	46	
			Oxalate	1	5	20	60	..	...	.....	..	..	..	..	..	..	10	30	
			Heparin	2	10	43	75	82	460	8,400	38	45	12	2	3	..	21.5	37.5	7/ 7/28

F. F.	M	8	Citrate.....	3	8	15	84	..	...	.....	..	..	..	..	..	..	7.5	42	
			Oxalate.....	15	42	80	101	..	...	.....	..	..	..	..	..	..	40	50.5	
			Heparin.....	..	..	..	..	84	471	10,400	55	41	4	..	..	..	..	....	4/21/28
			Citrate.....	0	3	10	60	..	...	.....	..	..	..	..	..	..	5	30	
			Oxalate.....	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Heparin.....	..	..	..	..	83	463	8,150	61	22	11	5	1	..	..	....	7/10/28
R. K.	F	5	Citrate.....	0	4	14	40	..	...	.....	..	..	..	..	..	..	7	20	
			Oxalate.....	0	6	24	53	..	...	.....	..	..	..	..	..	..	12	26.5	
			Heparin.....	0	34	78	93	78	437	9,450	51	33	6	9	1	..	39	46.5	4/ 7/28
			Citrate.....	0	1	18	94	..	...	.....	..	..	..	..	..	..	9	47	
			Oxalate.....	0	2	24	73	..	...	.....	..	..	..	..	..	..	12	36.5	
			Heparin.....	0	21	56	81	78	446	8,500	62	28	4	3	2	1	28	40.5	
V. S.	F	3	Citrate.....	0	7	25	73	..	...	.....	..	..	..	..	..	..	12.5	36.5	
			Oxalate.....	0	12	30	66	..	...	.....	..	..	..	..	..	..	15	33	
			Heparin.....	0	20	58	83	72	461	7,900	54	30	10	5	1	..	29	41.5	4/ 7/28
G. G.	M	5	Citrate.....	0	3	5	16	..	...	.....	..	..	..	..	..	..	2.5	8	
			Oxalate.....	0	5	18	41	..	...	.....	..	..	..	..	..	..	9	20.5	
			Heparin.....	0	18	30	86	82	467	10,250	59	24	9	6	2	..	15	43	4/ 7/28
			Citrate.....	0	3	12	92	..	...	.....	..	..	..	..	..	..	6	46	
			Oxalate.....	0	2	21	40	..	...	.....	..	..	..	..	..	..	10.5	20	
			Heparin.....	0	5	38	62	81	457	8,100	65	21	10	2	2	..	19	31	7/12/28
J. B.	M	4	Citrate.....	2	5	6	33	..	...	.....	..	..	..	..	..	..	3	16.5	
			Oxalate.....	0	2	8	75	..	...	.....	..	..	..	..	..	..	4	37.5	
			Heparin..... ..	..	..	..	..	77	445	10,9.0	48	40	7	4	1	..	..	....	4/ 7/28
			Citrate.....	0	1	8	82	..	...	.....	..	..	..	..	..	..	4	41	
			Oxalate.....	0	1	10	50	..	...	.....	..	..	..	..	..	..	5	25	
			Heparin.....	0	1	18	50	75	428	8,250	52	38	10	5	3	2	9	25	
O. S.	M	5	Citrate.....	3	5	15	70	..	...	.....	..	..	..	..	..	..	7.5	35	
			Oxalate.....	7	9	18	58	..	...	.....	..	..	..	..	..	..	9	29	
			Heparin.....	12	21	50	108	71	435	8,550	50	38	7	5	..	..	25	54	4/ 7/28
			Citrate.....	0	4	18	75	..	...	.....	..	..	..	..	..	..	9	37.5	
			Oxalate.....	0	5	21	63	..	...	.....	..	..	..	..	..	..	10.5	31.5	
			Heparin.....	0	8	43	100	77	468	8,000	62	20	10	5	3	..	21.5	50	
H. S.	M	7	Citrate.....	0	3	7	21	..	...	.....	..	..	..	..	..	..	3.5	10.5	
			Oxalate.....	1	2	9	98	..	...	.....	..	..	..	..	..	..	4.5	39	
			Heparin.....	0	18	49	110	85	460	10,000	54	38	8	..	..	..	24.5	55	4/ 7/28
			Citrate.....	1	5	11	55	..	...	.....	..	..	..	..	..	..	5.5	27.5	
			Oxalate.....	2	25	36	70	..	...	.....	..	..	..	..	..	..	18	35	
			Heparin..... .	3	35	49	80	81	468	8,900	64	12	12	2	10	..	24.5	40	
F. B.	M	7	Citrate.....	0	3	9	36	..	...	.....	..	..	..	..	..	..	4.5	18	
			Oxalate.....	1	3	24	48	..	...	.....	..	..	..	..	..	..	12	24	
			Heparin.....	1	4	21	63	80	461	9,150	56	40	4	..	..	..	10.5	31.5	4/ 7/28
			Citrate.....	0	0	10	24	..	...	.....	..	..	..	..	..	..	5	12	
			Oxalate.....	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Heparin.....	..	..	..	..	82	471	7,950	72	12	10	5	1	..	..	....	

TABLE 2.—*Sedimentation Rate in Normal Children—Continued*

Name	Sex	Age, Yrs.	Readings in Mm.	Sedimentation in Hours ½	1	2	24	Hemoglobin, per Cent	Red Blood Cells	White Blood Cells	Differential: Polymorphonuclears	Small Lymphocytes	Large Lymphocytes	Large Mononuclears	Transitionals	Eosinophils	Plasma, per Cent by Volume 2 Hrs.	24 Hrs.	Date
M. K.	F	10	Citrate	2	3	40	98	..	...	.....	..	..	..	..	..	..	20	49	
			Oxalate	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Heparin	..	..	..	..	82	461	8,230	68	21	5	3	2	1	..	....	7/10/28
M. B.	F	13	Citrate	0	5	15	36	..	...	.....	..	..	..	..	..	..	7.5	18	
			Oxalate	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Heparin	0	5	27	73	81	464	9,800	62	22	8	6	2	..	13.5	36.5	6/16/28
			Citrate	0	0	18	89	..	...	.....	..	..	..	..	..	.	9	41.5	
			Oxalate	0	1	14	32	..	...	.....	..	..	..	..	..	..	7	16	
			*Heparin	0	1	31	74	80	464	9,850	60	24	7	8	1	..	15.5	37	7/14/28
E. R.	F	14	Citrate	0	1	4	56	..	...	.....	..	..	..	..	..	..	2	28	
			Oxalate	0	1	2	30	..	...	.....	..	..	..	..	..	..	1	15	
			Heparin	0	2	10	58	80	461	9,350	66	24	8	2	..	..	5	29	6/16/28
Home																			
D. K.	F	..	Citrate	0	8	35	75	..	...	.....	..	..	..	..	..	.	17.5	37.5	
			Oxalate	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Heparin	..	..	..	..	78	451	9,700	58	40	2	..	..	..	..	....	6/16/28
			Citrate	0	1	28	87	..	...	.....	..	..	..	..	..	..	14	43.5	
			Oxalate	0	2	21	53	..	...	.....	..	..	..	..	..	..	10.5	26.5	
			*Heparin	..	3	24	79	81	462	8,550	69	25	5	6	3	..	12	39.5	7/14/28
M. K.	F	14	Citrate	0	6	20	83	..	...	.....	..	..	..	..	..	..	10	41.5	
			Oxalate	0	10	46	85	..	...	.....	..	..	..	..	..	..	23	42.5	
			Heparin	..	..	..	..	87	473	8,700	58	34	4	3	1	..	..	....	6/30/28
			Citrate	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Oxalate	0	3	41	68	..	...	.....	..	..	..	..	..	.	20.5	34	
			Heparin	0	8	48	88	85	481	8,750	60	28	6	5	1	..	24	44	7/14/28
C. H.	F	13	Citrate	3	4	20	70	..	...	.....	..	..	..	..	..	..	10	35	
			Oxalate	2	8	25	71	..	...	.....	..	..	..	..	..	..	12.5	35.5	
			Heparin	..	..	..	..	80	448	9,450	63	27	4	5	2	..	..	....	6/30/28
			Citrate	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Oxalate	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Heparin	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	7/16/28
V. S.	F	3	Citrate	0	0	21	84	..	...	.....	..	..	..	..	..	..	10.5	42	
			Oxalate	0	2	28	50	..	...	.....	..	..	..	..	..	..	14	25	
			Heparin	0	12	73	100	74	461	7,850	60	28	10	1	1	..	36.5	50	7/17/28
S. S.	F	4	Citrate	0	5	10	70	..	...	.....	..	..	..	..	..	..	5	35	
			Oxalate	0	15	40	66	..	...	.....	..	..	..	..	..	..	20	33	
			Heparin	0	15	45	93	77	456	10,000	48	44	4	3	1	..	22.5	46.5	4/ 7/28

			Citrate.....	0	2	18	84	..	...	.....	..	..	..	..	..	..	9	42	
			Oxalate.....	0	3	38	61	..	...	.....	..	..	..	..	..	..	19	30.5	
			Heparin.....	..	..	..	..	78	456	8,595	52	24	4	5	3	2	..	....	7/17/28
M. J.	F	6	Citrate.....	0	7	18	83	..	...	.....	..	..	..	..	..	..	9	41.5	
			Oxalate.....	0	7	30	67	..	...	.....	..	..	..	..	..	..	15	33.5	
			Heparin.....	0	13	33	85	75	482	8,850	60	26	5	6	2	1	16.5	42.5	4/ 7/28
			Citrate.....	0	1	38	91	..	...	.....	..	..	..	..	..	..	19	45.5	
			Oxalate.....	1	3	21	70	..	...	.....	..	..	..	..	..	..	10.5	35	
			Heparin.....	..	..	..	..	80	462	8,300	65	20	7	5	1	3	..	....	7/14/28
V. H.	F	13	Citrate.....	5	10	25	80	..	...	.....	..	..	..	..	..	..	12.5	40	
			Oxalate.....	2	7	32	65	..	...	.....	..	..	..	..	..	..	16	32.5	
			Heparin.....	10	37	83	98	85	501	9,050	44	26	20	2	3	5	41.5	49	4/14/28
		Home																	
A. M.	F	14	Citrate.....	5	10	12	60	..	...	.....	..	..	..	..	..	..	6	30	
			Oxalate.....	0	0	5	75	..	...	.....	..	..	..	..	..	..	2.5	37.5	
			Heparin.....	6	15	49	82	87	486	9,900	50	29	1	1	..	..	24.5	41	
		Home																	
E. S.	F	6	Citrate.....	0	10	35	73	..	...	.....	..	..	..	..	..	..	17.5	36.5	
			Oxalate.....	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Heparin.....	..	..	..	..	82	456	10,050	60	24	8	4	2	..	..	....	7/12/28
			Citrate.....	0	0	36	85	..	...	.....	..	..	..	..	..	..	18	42.5	
			Oxalate.....	0	2	21	60	..	...	.....	..	..	..	..	..	..	10.5	30	
			Heparin.....	..	..	..	..	85	477	7,800	62	26	4	4	2	..	..	....	
G. H.	F	9	Citrate.....	0	5	12	75	..	...	.....	..	..	..	..	..	..	6	37.5	
			Oxalate.....	1	8	15	53	..	...	.....	..	..	..	..	..	..	7.5	26.5	
			Heparin.....	5	40	65	105	78	459	10,000	55	38	5	1	1	..	32.5	52.5	5/ 5/28
			Citrate.....	0	0	37	95	..	...	.....	..	..	..	..	..	..	18.5	47.5	
			Oxalate.....	0	1	28	90	..	...	.....	..	..	..	..	..	..	14	45	
			Heparin.....	0	5	37	94	81	461	7,950	61	28	10	1	..	..	18.5	47	
A. B.	F	12	Citrate.....	0	2	3	45	..	...	.....	..	..	..	..	..	..	1.5	22.5	
			Oxylate.....	1	5	13	35	..	...	.....	..	..	..	..	..	..	6.5	17.5	
			Heparin.....	0	5	12	65	83	470	7,800	68	26	4	1	1	..	6	32.5	5/ 5/28
			Citrate.....	0	3	21	56	..	...	.....	..	..	..	..	..	..	10.5	28	
			Oxalate.....	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Heparin.....	..	..	..	..	85	465	8,150	65	21	12	..	2	..	..	....	7/11/28
B. P.	F	12	Citrate.....	0	10	18	50	..	...	.....	..	..	..	..	..	..	9	25	
			Oxalate.....	1	5	15	63	..	...	.....	..	..	..	..	..	..	7.5	31.5	
			Heparin.....	1	24	56	90	82	459	8,350	67	30	2	1	..	..	27.5	45	5/ 5/28
		Home																	
J. F.	F	9	Citrate.....	0	0	15	60	..	...	.....	..	..	..	..	..	..	7.5	30	
			Oxalate.....	1	15	25	80	..	...	.....	..	..	..	..	..	..	12.5	40	
			Heparin.....	1	25	48	95	88	472	7,700	52	44	2	2	..	..	24	47.5	5/ 5/28

* One per cent basophils.

TABLE 2.—*Sedimentation Rate in Normal Children—Continued*

Name	Sex	Age, Yrs.	Readings in Mm.	Sedimentation in Hours ½	1	2	24	Hemoglobin, per Cent	Red Blood Cells	White Blood Cells	Differential: Polymorphonuclears	Small Lymphocytes	Large Lymphocytes	Large Mononuclears	Transitionals	Eosinophils	Plasma, per Cent by Volume 2 Hrs.	24 Hrs.	Date
			Citrate	0	0	51	100	..	...	.....	..	..	..	..	..	..	25.5	50	
			Oxalate	0	1	32	50	..	...	.....	..	..	..	..	..	..	16	25	
			Heparin	0	2	18	38	85	457	8,200	71	21	4	2	2	..	9	19	7/14/28
G. F.	F	10	Citrate	1	5	15	20	..	...	.....	..	..	..	..	..	..	7.5	10	
			Oxalate	1	10	23	70	..	...	.....	..	..	..	..	..	..	11.5	35	
			Heparin	0	22	43	80	82	475	8,250	68	21	5	5	1	..	21.5	40	5/ 5/28
			Citrate	0	2	21	90	..	...	.....	..	..	..	..	..	..	10.5	45	
			Oxalate	0	12	31	90	..	...	.....	..	..	..	..	..	..	15.5	45	
			Heparin	..	..	..	..	80	467	8,050	64	25	5	2	6	..	..	....	7/13/28
M. K.	F	10	Citrate	0	15	40	73	..	...	.....	..	..	..	..	..	..	20	36.5	
			Oxalate	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Heparin	..	..	..	..	80	465	7,600	58	32	8	1	1	.	..	....	6/ 5/28
E. K.	F	11	Citrate	0	4	12	93	..	...	.....	..	..	..	..	..	..	6	46.5	
			Oxalate	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Heparin	..	..	..	..	82	462	7,950	62	22	8	6	2	..	..	....	7/11/28
			Citrate	0	2	28	110	..	...	.....	..	..	..	..	..	..	14	55	
			Oxalate	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			Heparin	..	..	..	..	82	470	8,300	61	20	8	6	2	1	..	....	7/14/28
C. T.	M	6	Citrate	0	4	12	82	..	...	.....	..	..	..	..	..	..	6	41	
			Oxalate	1	6	21	87	..	...	.....	..	..	..	..	..	..	10.5	43.5	
			Heparin	3	10	30	91	80	465	8,100	62	25	10	1	2	..	15	45.5	6/11/28
Home																			
C. F.	M	9	Citrate	1	2	5	50	..	...	.....	..	..	..	..	..	..	2.5	25	
			Oxalate	2	12	31	54	..	...	.....	..	..	..	..	..	..	15.5	27	
			Heparin	2	15	50	74	83	461	8,400	58	18	10	8	4	2	25	37	6/30/28
			Citrate	0	6	35	89	..	...	.....	..	..	..	..	..	..	17.5	44.5	
			Oxalate	1	8	19	40	..	...	.....	..	..	..	..	..	..	9.5	20	
			Heparin	0	12	28	68	81	470	8,450	68	10	5	3	5	8	14	34	7/11/28
L. R.	M	11	Citrate	0	5	15	72	..	...	.....	..	..	..	..	..	..	7.5	36	
			Oxalate	0	11	32	53	..	...	.....	..	..	..	..	..	..	16	26.5	
			Heparin	3	35	68	81	78	463	8,500	61	31	4	2	2	..	34	40.5	6/30/28
			Citrate	0	7	17	73	..	...	.....	..	..	..	..	..	..	8.5	36.5	
			Oxalate	0	0	8	45	..	...	.....	..	..	..	..	..	..	4	22.5	
			Heparin	1	2	18	92	80	451	8,250	70	22	4	2	3	1	9	46	7/11/28
G. S.	M	..	Citrate	0	5	31	90	..	...	.....	..	..	..	..	..	..	15.5	45	
			Oxalate	0	10	40	96	..	...	.....	..	..	..	..	..	..	20	48	
			Heparin	3	20	24	97	88	478	8,050	66	20	8	3	3	..	12	48.5	6/30/28

			Citrate.....	0	7	38	91	..	...	.....	..	..	..	..	..	..	19	45.5	
			Oxalate.....	2	11	24	55	..	...	.....	..	..	..	..	..	..	12	27.5	
			Heparin.....	0	9	18	55	82	471	9,250	71	18	5	3	3	..	9	27.5	7/11/28
M. K.	F	8	Citrate.....	0	0	2	24	..	...	.....	..	..	..	..	..	..	1	12	
			Oxalate.....	0	5	24	60	..	...	.....	..	..	..	..	..	..	12	30	
			Heparin.....	1	10	45	88	89	488	8,150	70	21	7	2	..	..	22.5	44	4/28/28
Home																			
V. B.	F	9	Citrate.....	0	3	12	60	..	...	.....	..	..	..	..	..	..	6	30	
			Oxalate.....	0	4	20	45	..	...	.....	..	..	..	..	..	..	10	22.5	
			Heparin.....	0	2	20	83	81	458	8,250	66	21	10	2	1	..	10	41.5	4/28/28
			Citrate.....	0	1	18	75	..	...	.....	..	..	..	..	..	..	9	37.5	
			Oxalate.....	0	2	21	50	..	...	.....	..	..	..	..	..	..	10.5	25	
			Heparin.....	0	3	18	73	81	464	10,000	68	20	10	4	6	..	9	36.5	7/11/28
M. W.	F	9	Citrate.....	0	3	16	50	..	...	.....	..	..	..	..	..	..	8	25	
			Oxalate.....	1	5	10	30	..	...	.....	..	..	..	..	..	..	5	15	
			Heparin.....	5	18	35	80	82	462	10,200	73	17	5	4	1	..	17.5	40	4/28/28
			Citrate.....	0	0	14	67	..	...	.....	..	..	..	..	..	..	7	33.5	
			Oxalate.....	0	0	38	50	..	...	.....	..	..	..	..	..	..	19	25	
			Heparin.....	0	2	32	82	81	457	9,600	70	20	5	3	2	..	16	41	7/11/28
E. M.	F	9	Citrate.....	0	0	4	55	..	...	.....	..	..	..	..	..	..	2	27.5	
			Oxalate.....	0	5	16	47	..	...	.....	..	..	..	..	..	..	8	23.5	
			Heparin.....	1	5	34	86	83	456	8,450	61	26	9	3	..	1	17	43	4/28/28
			Citrate.....	0	0	8	60	..	...	.....	..	..	..	..	..	..	4	30	
			Oxalate.....	0	0	16	63	..	...	.....	..	..	..	..	..	..	8	31.5	
			Heparin.....	0	2	21	81	81	463	8,600	60	20	11	5	2	2	10.5	40.5	7/12/28
H. M.	F	8	Citrate.....	0	9	15	70	..	...	.....	..	..	..	..	..	..	7.5	35	
			Oxalate.....	4	15	40	65	..	...	.....	..	..	..	..	..	..	20	32.5	
			Heparin.....	3	25	70	100	77	457	10,900	70	15	10	3	2	..	35	50	
Home																			
D. M.	M	12	Citrate.....	0	3	18	52	..	...	.....	..	..	..	..	..	..	9	23	
			Oxalate.....	0	5	25	61	..	...	.....	..	..	..	..	..	..	12.5	30.5	
			*Heparin.....	2	10	40	69	78	464	8,950	63	26	10	..	..	..	20	34.5	6/16/28
			Citrate.....	0	1	21	80	..	...	.....	..	..	..	..	..	..	10.5	40	
			Oxalate.....	0	2	26	45	..	...	.....	..	..	..	..	..	..	13	22.5	
			*Heparin.....	0	0	52	86	78	481	8,850	60	24	10	2	1	..	16	43	7/14/28
E. M.	M	13	Citrate.....	0	3	10	68	..	...	.....	..	..	..	..	..	..	5	34	
			Oxalate.....	0	4	12	42	..	...	.....	..	..	..	..	..	..	6	21	
			Heparin.....	3	15	42	87	85	467	8,000	56	31	3	6	4	..	21	43.5	6/16/28
Home																			
R. M.	M	14	Citrate.....	2	5	22	70	..	...	.....	..	..	..	..	..	..	11	35	
			Oxalate.....	0	5	24	50	..	...	.....	..	..	..	..	..	..	12	25	
			Heparin.....	..	..	..	..	88	492	7,800	58	22	10	4	6	..	..	....	7/ 7/28

* One per cent basophils.

TABLE 2.—*Sedimentation Rate in Normal Children—Continued*

Name	Sex	Age, Yrs.	Readings in Mm.	Sedimentation in Hours: ½	1	2	24	Hemoglobin, per Cent	Red Blood Cells	White Blood Cells	Differential: Polymorphonuclears	Small Lymphocytes	Large Lymphocytes	Large Mononuclears	Transitionals	Eosinophils	Plasma, per Cent by Volume: 2 Hrs.	24 Hrs.	Date
			Citrate.....	0	1	18	74	..	...	.....	..	..	..	..	..	..	9	37	
			Oxalate.....	0	2	21	55	..	...	.....	..	..	..	..	..	..	10.5	27.5	
			*Heparin.....	0	3	32	77	87	476	9,050	61	20	9	3	7	..	16	38.5	7/14/28
J. J.	M	13	Citrate.....	0	3	16	70	..	...	.....	..	..	..	..	..	..	8	35	
			Oxalate.....	4	12	38	68	..	...	.....	..	..	..	..	..	..	19	34	
			Heparin.....	5	20	72	90	82	472	8,100	65	21	7	7	..	..	36	45	7/ 7/28
			Citrate.....	0	2	32	90	..	...	.....	..	..	..	..	..	..	16	45	
			Oxalate.....	0	3	48	82	..	...	.....	..	..	..	..	..	..	24	41	
			Heparin.....	..	..	..	..	82	493	9,450	63	20	10	6	1	..	..	....	7/14/28
G. W.	M	13	Citrate.....	0	1	10	70	..	...	.....	..	..	..	..	..	..	5	35	
			Oxalate.....	0	5	20	50	..	...	.....	..	..	..	..	..	..	10	25	
			Heparin.....	2	8	33	70	86	484	8,500	72	11	9	6	2	..	16.5	35	7/ 7/28
			Citrate.....	0	5	12	68	..	...	.....	..	..	..	..	..	..	6	34	
			Oxalate.....	2	8	24	50	..	...	.....	..	..	..	..	..	..	12	25	
			Heparin.....	3	10	38	78	88	502	8,260	75	21	3	1	..	..	19	39	
C. S.	M	6	Citrate.....	1	4	11	45	..	...	.....	..	..	..	..	..	..	5.5	22.5	
			Oxalate.....	1	2	15	50	..	...	.....	..	..	..	..	..	..	7.5	25	
			Heparin.....	..	..	..	..	78	459	9,150	52	36	12	..	..	..	..	....	4/ 7/28
			Citrate.....	0	5	23	70	..	...	.....	..	..	..	..	..	..	11.5	35	
			Oxalate.....	0	0	8	32	..	...	.....	..	..	..	..	..	..	4	16	
			Heparin.....	..	..	..	..	82	467	8,500	61	18	10	5	6	..	..	....	
E. R.	M	6	Citrate.....	0	5	8	60	..	...	.....	..	..	..	..	..	..	4	30	
			Oxalate.....	0	28	81	93	..	...	.....	..	..	..	..	..	.	40.5	46.5	
			Heparin.....	0	14	90	110	82	451	10,000	68	22	4	4	2	..	45	55	4/14/28
Home																			
G. R.	M	9	Citrate.....	0	5	7	61	..	...	.....	..	..	..	..	..	..	3.5	30.5	
			Oxalate.....	8	20	58	110	..	...	.....	..	..	..	..	..	..	29	55	
			Heparin.....	12	30	71	108	83	461	9,300	66	34	..	..	..	..	35.5	54	4/14/28
Home																			
R. R.	M	7	Citrate.....	1	4	12	63	..	...	.....	..	..	..	..	..	..	6	33	
			Oxalate.....	1	8	30	46	..	...	.....	..	..	..	..	..	..	15	23	
			Heparin.....	1	14	50	87	82	470	11,550	53	43	4	..	..	..	25	43.5	4/14/28
			Citrate.....	0	6	21	72	..	...	.....	..	..	..	..	..	..	10.5	36	
			Oxalate.....	0	8	28	51	..	...	.....	..	..	..	..	..	..	14	25.5	
			Heparin.....	0	20	48	91	80	462	10,150	58	36	5	1	..	..	24	45.5	7/10/28

R. R.	M	6	Citrate.....	0	0	5	60	..	...	.....	..	..	..	..	..	..	2.5	30	
			Oxalate.....	2	8	30	67	..	...	.....	..	..	..	..	..	..	15	33.5	
			Heparin.....	10	45	90	108	77	464	9,650	43	54	3	..	..	..	45	54	4/14/28
			Citrate.....	0	5	18	85	..	...	.....	..	..	..	..	..	..	9	42.5	
			Oxalate.....	0	10	31	50	..	...	.....	..	..	..	..	..	..	15.5	25	
			Heparin.....	1	24	48	83	82	463	8,900	41	58	..	1	..	..	24	41.5	7/10/28
R. S.	M	6	Citrate.....	1	2	5	70	..	...	.....	..	..	..	..	..	..	2.5	35	
			Oxalate.....	4	11	40	76	..	...	.....	..	..	..	..	..	..	20	38	
			Heparin.....	10	25	66	100	81	454	10,550	60	35	3	2	..	..	33	50	4/14/28
R. S.	M	8	Citrate.....	10	20	45	76	..	...	.....	..	..	..	..	..	..	22.5	38	
			Oxalate.....	8	23	53	86	..	...	.....	..	..	..	..	..	..	26.5	43	
			Heparin.....	..	..	..	..	81	462	9,700	40	54	4	2	..	..	..	....	4/14/28
Home																			
I. S.	M	6	Citrate.....	1	2	5	70	..	...	.....	..	..	..	..	..	..	2.5	35	
			Oxalate.....	4	11	40	76	..	...	.....	..	..	..	..	..	..	20	38	
			Heparin.....	10	25	66	100	81	454	10,550	60	35	3	2	..	..	33	50	4/14/28
			Citrate.....	0	5	32	82	..	...	.....	..	..	..	..	..	..	16	41	
			Oxalate.....	0	8	45	70	..	...	.....	..	..	..	..	..	..	22.5	35	
			Heparin.....	..	..	..	..	85	487	9,650	72	25	1	2	..	..	..	....	
M. F.	M	8	Citrate.....	4	10	38	80	..	...	.....	..	..	..	..	..	..	19	40	
			Oxalate.....	16	31	53	80	..	...	.....	..	..	..	..	..	..	26.5	40	
			Heparin.....	25	55	89	97	78	455	9,700	60	35	6	1	..	.	44.5	48.5	4/21/28
			Citrate.....	0	2	18	31	..	...	.....	..	..	..	..	..	.	9	15.5	
			Oxalate.....	8	32	62	93	..	...	.....	..	..	..	..	..	..	31	46.5	
			Heparin.....	21	61	89	101	81	463	9,850	71	25	2	1	1	..	44.5	50.5	7/ 9/28
J. N.	M	7	Citrate.....	2	6	22	83	..	...	.....	..	..	..	..	..	..	11	41.5	
			Oxalate.....	7	28	50	80	..	...	.....	..	..	..	..	..	..	25	40	
			Heparin.....	9	26	48	80	71	455	11,800	68	25	6	1	..	..	24	40	4/21/28
			Citrate.....	0	5	32	85	..	...	.....	..	..	..	..	..	..	16	42.5	
			Oxalate.....	0	2	20	56	..	...	.....	..	..	..	..	..	..	10	28	
			Heparin.....	..	..	..	..	78	472	10,100	72	24	2	1	1	..	..	....	
P. N.	M	6	Citrate.....	2	6	15	80	..	...	.....	..	..	..	..	..	..	7.5	40	
			Oxalate.....	7	20	45	65	..	...	.....	..	..	..	..	..	..	22.5	32.5	
			Heparin.....	10	37	67	85	78	452	9,650	49	34	14	3	..	..	33.5	42.5	4/21/28
			Citrate.....	0	5	15	88	..	...	.....	..	..	..	..	..	..	7.5	44	
			Oxalate.....	..	..	..	..	..	...	.....	..	..	..	..	..	..	..	....	
			*Heparin.....	..	..	..	..	76	448	8,750	52	34	10	2	..	1	..	....	
G. B.	M	6	Citrate.....	3	8	20	63	..	...	.....	..	..	..	..	..	..	10	31.5	
			Oxalate.....	4	10	30	55	..	...	.....	..	..	..	..	..	.	15	27.5	
			Heparin.....	6	22	40	75	80	466	10,150	22	69	9	..	..	..	20	37.5	4/21/28

* One per cent basophils.

22 C., and refrigerator temperature, 2 C., for varying periods (table 5 and chart 3). In another series of experiments, red cells taken from well children with normal sedimentation rates were placed in blood serums taken from sick children with rapid rates. This procedure was then reversed. Next the red cells of both were washed in physiologic sodium chloride solution and the procedures repeated (table 6). Four hundred and thirty-three determinations were then made on patients in the hospital suffering from tuberculosis of the bones and joints, osteo-

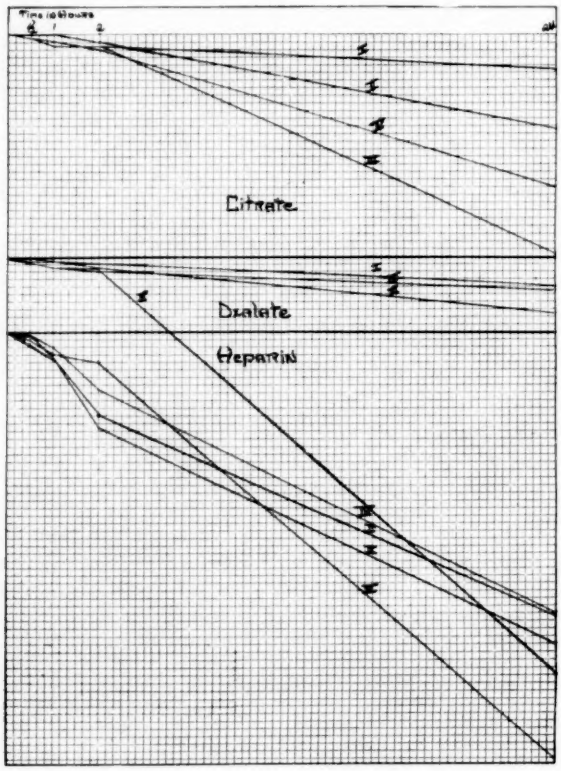

Chart 2.—Daily variations in normal adult. *I* indicates before breakfast (8 a. m.); *II*, before lunch (10:30 a. m.); *III*, after lunch, 1 p. m., and *IV*, late afternoon (4:30 p. m.). The variations in the blood were read in millimeters, each space representing 2 mm.

myelitis, mastoiditis, fractures, contusions, acute arthritis, malignant tumor, tumor of the brain, hemangioma, puncture wounds, cellulitis, acute appendicitis, peritonitis, septicemia, empyema, burns, tonsillitis, bronchopneumonia, meningitis (tuberculous, meningococcic and streptococcic), chorea, encephalitis, pertussis, scarlet fever, mumps, pyelocystitis, intestinal ulceration, rachitis, secondary anemia, alimentary

intoxication, cardiac disease, celiac disease, hepatic chirrhosis, epilepsy and diabetes. In the treatment of sick children there are obviously a number of factors which limit the number and extent of examinations which may be made for diagnosis and prognosis. In a number of cases we obtained blood for determination of only one sedimentation rate. Hence our preliminary studies are not as complete as we should desire. We shall present in this communication only those observations which demonstrate the essential features of our results.

COMMENT

We have not attempted to draw extensive conclusions from this small series of cases. However, a study of our material reveals some interesting points. If we leave out of consideration the variation to be expected in the various methods of technic, the amount of blood, the size and bore of the tube used and the height of the column of blood, there are many other factors which influence the sedimentation rate.

TABLE 3.—*Sedimentation Rate in Normal Infants*

	Age	Sex		½ Hour	1 Hour	2 Hours	24 Hours
1	4 weeks	M	Citarte	1	2	2	40
2	5 weeks	F	Citrate	0	1	1	58
3	7 weeks	F	Citrate	2	3	5	20
4	8 weeks	M	Citrate	2	3	5	130
5	2 months	F	Citrate	2	4	7	96

We have illustrated the great variations effected by the anticoagulants. Not only the dilution factor but the electrolytes produce extreme variations. The time elapsing after the blood is taken and the temperature conditions under which the blood is kept and the test is made exert inconstant and irregular influences. If we add to these irregularities the variations in the rate as demonstrated in normal persons, the evaluations of the sedimentation rate become confusing. Either one must allow a wide range of variations in the normal and thus include, as may be seen in tables 8 and 9, fatal diseases, or establish narrow limits in the normal and sacrifice specificity. One single determination of the sedimentation rate has been of little value in diagnosis and of no value in prognosis in our studies. We have obtained rapid sedimentation rates in patients recovering from acute illnesses with normal blood counts and temperatures whose conditions were clinically good. We have noted "normal" or low rates in sick children just before death. In secondary anemia, in which most investigators report a decreased rate, our citrate readings have also been slow unless there was associated an active acute inflammation. R. L. (table 7) who was acutely ill with Meckel's diver-

TABLE 4.—*Sedimentation Rate in Normal Adults Showing Influence of Time and Meals*

Name	Time	Readings in Mm.	Sedimentation in Hours ½	1	2	24	Hemoglobin, per Cent	Red Blood Cells in Millions	White Blood Cells	Differential: Polymorphonuclears	Small Lymphocytes	Large Lymphocytes	Large Mononuclears	Transitionals	Clotting Time, Min.	Bleeding Time, Min.	Plasma, per Cent by Volume: 2 Hours	24 Hours
R. L.	Before breakfast, 8 a.m.	Citrate	1	3	3	9	88	5.80	11,900	70	17	8	4	1	2½	1	1.5	4.5
		Oxalate	0	1	2	8	..	....	.....	..	..	..	..	..	..	..	1	4
		Heparin	1	7	22	74	..	....	.....	..	..	..	..	..	..	..	11	37
	Before lunch, 11 a.m.	Citrate	0	0	2	25	..	....	.....	..	..	..	..	..	..	..	1	12.5
		Oxalate	0.5	1	3	15	..	....	.....	..	..	..	..	..	..	..	1.5	7.5
		Heparin	3	7	25	82	..	....	.....	..	..	..	..	..	..	..	12.5	41
	After lunch, 1:30 p.m.	Citrate	1	3	3	57	..	....	.....	..	..	..	..	..	..	..	1.5	28.5
		Oxalate	1	3	3	110	..	....	.....	..	..	..	..	..	..	..	1.5	55
		Heparin	2	6	8	112	..	....	.....	..	..	..	..	..	..	..	4	56
	Late afternoon, 4 p.m.	Citrate	1	2	4	40	..	....	.....	..	..	..	..	..	..	..	2	20
		Oxalate	1	3	4	9	..	....	.....	..	..	..	..	..	..	..	2	4.5
		Heparin	0	4	15	75	..	....	.....	..	..	..	..	..	..	..	7.5	37.5
M. S.	Before breakfast, 8 a.m.	Citrate	1	2	3	10	89	4.92	7,900	76	10	8	2	2	4	1½	1.5	5
		Oxalate	1	2	3	19	..	....	.....	..	..	..	..	..	..	..	1.5	9.5
		Heparin	0	2	5	75	..	....	.....	..	..	..	..	..	..	..	2.5	37.5
	Before lunch, 11 a.m.	Citrate	2	3	7	34	..	....	.....	..	..	..	..	..	..	..	3.5	17
		Oxalate	2	2	8	26	..	....	.....	..	..	..	..	..	..	..	4	13
		Heparin	1	7	37	95	..	....	.....	..	..	..	..	..	..	..	18.5	47.5
	After lunch, 1:30 p.m.	Citrate	1	3	4	22	..	....	.....	..	..	..	..	..	..	..	2	11
		Oxalate	0	0	2	35	..	....	.....	..	..	..	..	..	..	..	1	17.5
		Heparin	3	4	18	80	..	....	.....	..	..	..	..	..	..	..	9	40
	Late afternoon, 4 p.m.	Citrate	1	2	15	52	..	....	.....	..	..	..	..	..	..	..	7.5	26
		Oxalate	2	3	7	25	..	....	.....	..	..	..	..	..	..	..	3.5	12.5
		Heparin	3	5	10	62	..	....	.....	..	..	..	..	..	..	..	5	31
E. T.	Before breakfast, 8 a.m.	Citrate	1	1	3	25	92	4.64	8,650	78	19	6	4	2	3½	1½	1.5	12.5
		Oxalate	1	2	3	31	..	....	.....	..	..	..	..	..	..	..	1.5	15.5
		Heparin	3	4	23	87	..	....	.....	..	..	..	..	..	..	..	11.5	43.5
	Before lunch, 11 a.m.	Citrate	0	0	6	34	..	....	.....	..	..	..	..	..	..	..	3	17
		Oxalate	1	1.5	5	38	..	....	.....	..	..	..	..	..	..	..	2.5	19
		Heparin	1	4	20	78	..	....	.....	..	..	..	..	..	..	..	10	39
	After lunch, 4:30 p.m.	Citrate	0	1	3	37	..	....	.....	..	..	..	..	..	..	..	1.5	18.5
		Oxalate	0	1	4	47	..	....	.....	..	..	..	..	..	..	..	2	23.5
		Heparin	3	9	32	94	..	....	.....	..	..	..	..	..	..	..	16	47

M. S.	Before breakfast, 8 a.m.....	Citrate.....	1	2	6	17	86	4.69	12,900	68	28	2	2	..	4	1½	3	8.5
		Oxalate.....	1	3	13	42	..	....	.....	..	..	..	..	..	..	..	6.5	21
		Heparin.....	5	15	55	104	..	....	.....	..	..	..	..	..	..	..	27.5	52
	Before lunch, 11 a.m.....	Citrate.....	1	..	..	..	..	....	.....	..	..	..	..	..	..	..	...	....
		Oxalate.....	3	4.5	10	54	..	....	.....	..	..	..	..	..	..	..	5	27
		Heparin.....	9	15	15	90	..	....	.....	..	..	..	..	..	..	..	7.5	45
	After lunch, 1:30 p.m.....	Citrate.....	3	3	3	40	..	....	.....	..	..	..	..	..	..	..	1.5	20
		Oxalate.....	4	..	..	..	..	....	.....	..	..	..	..	..	..	..	...	....
		Heparin.....	1	2	7	91	..	....	.....	..	..	..	..	..	..	..	3.5	45.5
	Late afternoon, 4 p.m.....	Citrate.....	2	2	5	90	..	....	.....	..	..	..	..	..	..	..	2.5	45
		Oxalate.....	3	8	21	68	..	....	.....	..	..	..	..	..	..	..	10.5	34
		Heparin.....	3	25	56	105	..	....	.....	..	..	..	..	..	..	..	28	52.5
R. R.	Before breakfast, 8 a.m.....	Citrate.....	1	4	8	47	78	4.65	8,800	74	16	5	3	2	3½	1	4	23.5
		Oxalate.....	..	..	..	..	..	....	.....	..	..	..	..	..	..	..	...	....
		Heparin.....	1	5	12	70	..	....	.....	..	..	..	..	..	..	..	6	35
	Before lunch, 11 a.m.....	Citrate.....	1	..	7	32	..	....	.....	..	..	..	..	..	..	..	3.5	16
		Oxalate.....	0	..	6	52	..	....	.....	..	..	..	..	..	..	..	3	26
		Heparin.....	14	..	52	92	..	....	.....	..	..	..	..	..	..	..	26	46
	After lunch, 1:30 p.m.....	Citrate.....	0	1	3	37	..	....	.....	..	..	..	..	..	..	..	1.5	18.5
		Oxalate.....	0	3	11	60	..	....	.....	..	..	..	..	..	..	..	5.5	30
		Heparin.....	0	2	15	80	..	....	.....	..	..	..	..	..	..	..	7.5	40
	Late afternoon, 4 p.m.....	Citrate.....	1	2	3	61	..	....	.....	..	..	..	..	..	..	..	1.5	30.5
		Oxalate.....	..	3	5	35	..	....	.....	..	..	..	..	..	..	..	2.5	17.5
		Heparin.....	2	7	7	103	..	....	.....	..	..	..	..	..	..	..	3.5	51.5
E. M.	Before breakfast, 8 a.m.....	Citrate.....	4	5	15	56	88	5.06	10,650	74	16	6	3	1	5	2	7.5	28
		Oxalate.....	1	3	6	23	..	....	.....	..	..	..	..	..	..	..	3	11.5
		Heparin.....	0	0	5	71	..	....	.....	..	..	..	..	..	..	..	2.5	35.5
	Before lunch, 11 a.m.....	Citrate.....	1.5	4.5	15	54	..	....	.....	..	..	..	..	..	..	..	7.5	27
		Oxalate.....	4.5	7	26	53	..	....	.....	..	..	..	..	..	..	..	13	26.5
		Heparin.....	6	28	71	94	..	....	.....	..	..	..	..	..	..	..	35.5	47
	After lunch, 1:30 p.m.....	Citrate.....	1	6	14	56	..	....	.....	..	..	..	..	..	..	..	7	28
		Oxalate.....	..	..	..	..	..	....	.....	..	..	..	..	..	..	..	...	....
		Heparin.....	0	19	49	83	..	....	.....	..	..	..	..	..	..	..	24.5	41.5
	Late afternoon, 4 p.m.....	Citrate.....	2	5.5	12	57	..	....	.....	..	..	..	..	..	..	..	6	28.5
		Oxalate.....	2.5	9	17.5	37	..	....	.....	..	..	..	..	..	..	..	8.75	18.5
		Heparin.....	6	56	75	89	..	....	.....	..	..	..	..	..	..	..	37.5	44.5

TABLE 5.—*Influence of Temperature on Sedimentation Rate*

Name	Readings in	Sedimentation in Hours: ½ Mm	1	2	24	Hemoglobin, per Cent	Red Blood Cells in Millions	White Blood Cells	Differential: Polymorphonuclears	Small Lymphocytes	Large Lymphocytes	Large Mononuclears	Transitionals	Eosinophils	Basophils	Plasma, per Cent by Volume: 2 Hours	24 Hours
J. E.	Sedimentation rate *...	Citrate	4	12	28	107	60	3.98	6,150	62	30	6	2	..	..	..	14	53.5
		Oxalate	3	15	32	112	..	....	.....	..	..	..	..	..	..	..	16	56
		Heparin	5	22	40	120	..	....	.....	..	..	..	..	..	..	..	20	60
	Room temp. (37 to 38 C.), 1¼ hrs...		4	6	40	115	..	....	.....	..	..	..	..	..	..	..	20	57.5
	Icebox 6 C., 1¼ hrs...		3	6	40	111	..	....	.....	..	..	..	..	..	..	..	20	55.5
	Standing 24 hrs. at room temp. (37 C.)...		4	10	25	55	..	....	.....	..	..	..	..	..	..	..	12.5	27.5
	Standing 24 hrs. in icebox (6 C.)...		6	15	35	110	..	....	.....	..	..	..	..	..	..	..	17.5	58
	Standing 48 hrs. at room temp. (37 C.)...		0	0	3	16	..	....	.....	..	..	..	..	..	..	..	1.5	8
	Standing 48 hrs. in icebox (6 C.)...		4	21	40	118	..	....	.....	..	..	..	..	..	..	..	20	59
	Sedimentation, 3/1/28...	Citrate	6	11	26	104	..	....	.....	..	..	..	..	..	..	..	13	52
		Oxalate	10	24	48	104	..	....	.....	..	..	..	..	..	..	..	24	52
		Heparin	17	35	59	118	..	....	.....	..	..	..	..	..	..	..	29.5	59
	Incubator, 38 C...		3	8	14	112	..	....	.....	..	..	..	..	..	..	..	7	56
	Icebox, 6 C...		2	6	10	111	..	....	.....	..	..	..	..	..	..	..	5	55.5
	Sedimentation, 3/21/28...	Citrate	5	12	25	130	..	....	.....	..	..	..	..	..	..	..	12.5	65
		Oxalate	11	22	38	95	..	....	.....	..	..	..	..	..	..	..	19	47.5
		Heparin	5	11	34	105	..	....	.....	..	..	..	..	..	..	..	17	52.5
	Sedimentation, 4/2/28...	Citrate	4	15	27	103	..	....	.....	..	..	..	..	..	..	..	13.5	51.5
		Oxalate	5	22	42	104	..	....	.....	..	..	..	..	..	..	..	21	52
		Heparin	6	22	37	114	..	....	.....	..	..	..	..	..	..	..	18.5	57
W. K.	Sedimentation, 3/20/28...	Citrate	35	60	102	135	58	4.30	12,700	60	27	7	3	..	3	..	51	67.5
		Oxalate	54	75	110	130	..	....	.....	..	..	..	..	..	..	..	55	65
		Heparin	85	108	116	121	..	....	.....	..	..	..	..	..	..	..	58	60.5
	Incubator, 38 C...		10	20	51	121	..	....	.....	..	..	..	..	..	..	..	25.5	60.5
	Icebox, 6 C...		8	11	23	130	..	....	.....	..	..	..	..	..	..	..	11.5	65
	Sedimentation, 3/1/28...	Citrate	20	35	82	118	69	4.55	19,900	70	15	6	7	..	1	1	41	59
		Oxalate	39	71	101	110	..	....	.....	..	..	..	..	..	..	..	50.5	55
		Heparin	..	5	85	104	..	....	.....	..	..	..	..	..	..	..	42.5	52
	Sedimentation, 3/5/28...	Citrate	12	25	75	123	..	....	.....	..	..	..	..	..	..	..	37.5	61.5
		Oxalate	3	5	87	116	..	....	.....	..	..	..	..	..	..	..	43.5	58
		Heparin	4	10	90	103	..	....	.....	..	..	..	..	..	..	..	45	51.5
	Sedimentation, 3/12/28...	Citrate	12	60	94	125	..	....	.....	..	..	..	..	..	..	..	47	62.5
	Sedimentation, 3/16/28...	Citrate	20	55	91	127	..	....	.....	..	..	..	..	..	..	..	45.5	63.5
		Oxalate	33	74	112	121	..	....	.....	..	..	..	..	..	..	..	56	60.5
		Heparin	60	95	103	117	..	....	.....	..	..	..	..	..	..	..	51.5	58.5
J. G.	Sedimentation, 2/20/28...	Citrate	0	0	3	89	84	5.01	9,150	64	29	5	..	..	2	..	1.5	44.5
		Oxalate	1	3	5	43	..	....	.....	..	..	..	..	..	..	..	2.5	21.5
		Heparin	1.5	6	18	93	..	....	.....	..	..	..	..	..	..	..	9	46.5
	Standing at 37.5 C. in incubator...		0	1	3	13	..	....	.....	..	..	..	..	..	..	..	1.5	6.5
	Standing at room temp. for 24 hrs. (37 C.)...		1	3	6	35	..	....	.....	..	..	..	..	..	..	..	3	17.5
	Standing in icebox 24 hrs., then set up in room temperature...		2	4	8	62	..	....	.....	..	..	..	..	..	..	..	4	31
	Standing in icebox 24 hrs. (6 C.)...		0	1	3	53	..	....	.....	..	..	..	..	..	..	..	1.5	26.5

* When temperature is not specified, the test was made immediately at room temperature, from 37 to 38 C.

ticulum and ulceration of the mucosa (ileum) and bleeding, showed a rapid rate (citrate and heparin), and the sedimentation rates slowed down and paralleled his clinical condition as he improved. Table 8 presents data of three of the patients with bronchopneumonia who recovered. D. S. had a "normal" or slow rate (citrate) with a high leukocyte count; E. Y. had a rapid rate (citrate) with a normal leukocyte count, and P. G. a very rapid rate (citrate) with leukopenia. With D. S., the rate was confusing; in the case of P. G., who had leukopenia, it was of aid, indicating an acute process before the physical signs were detected.

W. K. (table 9), a healthy boy, was brought to the hospital with a fracture of one day's duration. His sedimentation rate (citrate) was

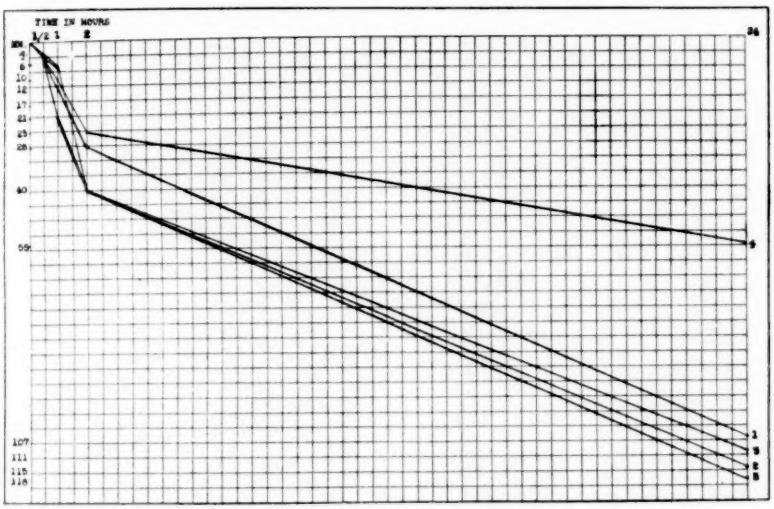

Chart 3.—Variations in normal blood at various temperatures.

increased and continued to increase four days later when his condition was good and the fracture reduced. Ten days later he developed abdominal pain and had a leukocytosis of 32,500, with 93 per cent polymorphonuclear cells; his rate (citrate) was normal. On the following day at operation a ruptured appendix and peritonitis were found. J. B., aged 5 years, included in this table, had a general peritonitis, and a rapid rate the day before death. J. B., aged 3 months, also in this table, with a malignant, ulcerating fibroblastoma under his chin (with metastasis to the glands) had a "normal" rate, while J. M., with a chancre on the tongue of six weeks' duration, had a rapid rate.

The cases of meningitis (table 10) illustrate extreme variations from slow to rapid rates with recovery, regardless of leukocyte counts. There is no distinction from meningismus.

The cases of chorea (table 11) also illustrate sedimentation rates which do not parallel the blood counts or the clinical course. The development of immunity to the disease in the recovery is not paralleled with an increased or a decreased rate.

The other cases illustrated are self explanatory. In all but the exceptional cases the leukocyte and differential counts, much more easily made, have been of far greater value in diagnosis and prognosis. Frequent leukocyte and differential counts offer a fairly comprehensive guide as to the progress of a case, whereas frequent determinations of sedimentation rates could offer little aid in most instances. In certain

TABLE 6.—*Interchange of Cells and Serums*

		Sedimentation Time in Hours			
		½	1	2	24
	Readings in Mm.				
W. B., sedimentation rapid	Citrate	39	85	125	145
	Oxalate	58	112	126	132
	Heparin	40	118	125	133
J. C., normal sedimentation	Citrate	5	15	30	62
	Oxalate	—	—	—	—
	Heparin	—	—	—	—
W. B., serum and J. C. cells	Citrate	45	80	122	147
J. C., serum and W. B. cells	Citrate	5	13	38	36
W. B., serum and J. C. cells washed	Citrate	18	55	70	132
J. C., serum and W. M. cells washed*	Citrate	1	5	9	93
W. B., serum and own cells washed*	Citrate	10	30	72	130
J. C., serum and own cells washed*	Citrate	7	22	52	110
A. N., normal sedimentation	Citrate	2	3	6	54
	Oxalate	4	8	17	61
	Heparin	12	21	36	97
B. W., normal sedimentation	Citrate	12	50	97	122
	Oxalate	30	73	110	123
	Heparin	45	100	107	112
B. W., serum and A. N. cells	Citrate	11	21	54	122
A. N., serum and B. W. cells	Citrate	2	6	22	65
B. W., serum and A. N. cells washed*	Citrate	0	1	2	20
A. N., serum and B. W. cells washed*	Citrate	1	3	3	18
B. W., cells and own serum washed*	Citrate	1	3	4	34
A. N., cells and own serum washed*	Citrate	0	1	2	15

* In physiologic sodium chloride solution.

cases in which other routine laboratory data are available, the sedimentation rate may offer additional support; on the other hand, when all other examinations give negative results, a rapid rate demands further search for an active process. The extreme variations noted in the citrate solution (dilution), oxalate powder (electrolyte) and heparin, in their effects on normal as well as on pathologic bloods, have not been satisfactorily interpreted. Suffice it to say that the twenty-four reading does not parallel the cell volume nor do the earlier readings parallel the clinical course.

It is probable that we have not exhausted the possibilities of value in the interpretation of our data. For that reason, our results are presented for discussion.

TABLE 7.—*Data of an Individual Case*

	Readings in Mm.	Sedimentation in Hours ½	1	2	24	Hemoglobin, per Cent	Red Blood Cells in Millions	White Blood Cells	Differential: Polymorphonuclears	Small Lymphocytes	Large Lymphocytes	Large Mononuclears	Transitionals	Plasma, per Cent by Volume: 2 Hours	24 Hours
R. L., a boy, aged 6 years; secondary anemia; Meckel's diverticulum with ulceration; duration of bleeding, 21 days	2/19—Citrate	20	30	80	127	52	3.55	10,250	72	20	4	4	..	40	63.5
	Oxalate	5	9	24	90	..	....	.....	..	..	..	..	..	12	45
	Heparin	50	75	118	140	..	....	.....	..	..	..	..	..	59	70
2/15/28, 500 cc. citrated blood															
2/19/28, 20 cc. whole blood intramuscularly	2/20—Citrate	12	25	60	115	59	3.55	13,650	..	.	..	..	..	30	57.5
	Oxalate	30	62	102	120	..	....	.....	..	..	..	..	..	51	60
2/22/28, 300 cc. citrated blood	Heparin	15	40	85	105	..	....	.....	..	..	..	..	..	42.5	52.5
2/24/28, resection of ileum															
3/ 2/28, improving; temperature practically normal except day of operation	3/ 2—Citrate	5	12	28	33	49	4.18	10,700	66	30	2	..	2	14	16.5
	Oxalate	7	20	58	74	..	....	.....	..	..	..	..	..	29	37
3/ 6/28, complete recovery	Heparin	13	33	75	105	..	....	.....	..	..	..	..	..	37.5	52.5
	3/ 6—Citrate	5	8	21	56	49	3.69	11,000	..	..	..	..	..	10.5	28
	Oxalate	12	18	70	112	..	....	.....	..	..	..	..	..	35	56
	Heparin	13	22	82	120	..	....	.....	..	..	..	..	..	41	60

TABLE 8.—*Sedimentation Rate in Bronchopneumonia*

	Readings in Mm.	Sedimentation in Hours ½	1	2	24	Hemoglobin, per Cent	Red Blood Cells in Millions	White Blood Cells	Differential: Polymorphonuclears	Small Lymphocytes	Large Lymphocytes	Large Mononuclears	Transitionals	Eosinophils	Plasma, per Cent by Volume: 2 Hours	24 Hours
D. S., a boy, aged 1 year; bronchopneumonia; duration, 10 days; temperature, 98.6; recovered	4/10/28—Citrate	0	4	10	36	80	4.12	21,000	60	39	..	1	..	..	5	18
	Oxalate	..	..	...	...	..	....	.....	..	..	..	..	..	..	....	....
	Heparin	..	..	...	...	..	....	.....	..	..	..	..	..	..	....	....
	4/12/28						....	14,560	35	46	19	..	..	..	....	....
	4/23/28						....	21,200	61	27	10	1	1	..	....	....
E. Y., a boy, aged 2 years; bronchopneumonia, mental deficiency; duration, 24 days (bronchopneumonia); 3/24/28, temperature, 101; given 3 Gm. thyroid extract; recovered from bronchopneumonia	3/24/28—Citrate	43	101	130	145	60	4.14	10,350	64	26	9	1	..	..	65	72.5
	Oxalate	..	..	...	...	..	....	.....	..	..	..	..	..	..	....	....
	Heparin	..	..	...	...	..	....	.....	..	..	..	.	..	..	....	....
P. G., a girl aged 1 year; bronchopneumonia; (mongolism); duration, 3 weeks; 2/9/28, recovered from bronchopneumonia	1/14/28—Citrate	40	72	108	108	74	4.63	5,050	41	46	10	1	..	2	54	54
	Oxalate	62	90	120	124	..	....	.....	..	..	..	..	..	..	60	62
	Heparin	111	119	128	128	..	....	.....	..	..	..	..	..	..	64	64

TABLE 9.—*Data of Sedimentation Rates*

	Readings in Mm.	Sedimentation in Hours ½	1	2	24	Hemoglobin, per Cent	Red Blood Cells in Millions	White Blood Cells	Differential: Polymorphonuclears	Small Lymphocytes	Large Lymphocytes	Large Mononuclears	Transitionals	Plasma, per Cent by Volume: 2 Hours	24 Hours
W. K., a boy, aged 8 years; fracture of left femur; ruptured appendix and peritonitis; duration, 27 days; temperature, 98.6; 3/17/28, legs in extension	3/15—Citrate	5	14	40	95	87	4.79	12,750	84	10	3	1	2	20	47.5
	Oxalate	8	18	40	68	..	....	.....	..	..	..	..	..	20	34
	Heparin	9	45	93	111	..	....	.....	..	..	..	..	..	46.5	55.5
Temperature, 98; condition good; 3/30/28, temperature, 102; abdominal pain	3/20—Citrate	17	35	66	110	79	5.56	32,500	93	..	5	1	1	33	55
	Oxalate	23	46	81	111	..	....	.....	..	..	..	..	..	40.5	55.5
	Heparin	18	48	101	113	..	....	.....	..	..	..	..	..	50.5	56.5
Operated on for ruptured appendix; condition poor; general peritonitis	3/31—Citrate	0	1	23	117	63	5.18	20,750	94	2	4	..	..	11.5	58.5
	Oxalate	0	1	48	80	..	....	.....	..	..	..	..	..	24	40
	Heparin	0	7	80	94	..	....	.....	..	..	..	..	..	40	47
Marked abdominal distention; condition poor	4/ 4—Citrate	45	76	105	128	60	4.55	23,100	..	..	..	..	..	52.5	64
	Oxalate	80	107	112	122	..	....	.....	..	..	.	..	..	56	61
	Heparin	20	81	93	105	..	....	.....	..	..	..	..	..	46.5	52.5
4/14/28, patient died	4/12—Citrate	9	24	55	93	..	....	.....	..	.	.	..	..	27.5	46.5
	Oxalate	20	49	73	120	..	....	.....	..	..	..	..	.	36.5	60
	Heparin	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
O. P., a girl, aged 11 years; acute tonsillitis with abdominal pain; duration, 3 days; temperature, 101	1/ 6—Citrate	12	24	56	121	83	5.16	17,300	66	7	10	3	4	28	60.5
	Oxalate	24	52	92	115	..	....	.....	..	..	..	..	..	46	57.5
	Heparin	28	71	96	111	..	....	.....	..	..	..	..	..	48	55.5
Temperature, 99.2; no pain; complete recovery	1/ 7—Citrate	7	36	50	118	..	....	.....	..	..	.	.	..	25	59
	Oxalate	2	30	46	110	..	....	.....	..	..	..	..	..	23	55
	Heparin	11	71	91	114	..	....	.....	..	..	..	..	..	45.5	57
J. B., a boy, aged 5 years; general peritonitis; scarlet fever 2 weeks previously; duration, 4 days; temperature, 102; 3/16/28, frequent emesis; 3/17/28, died	3/16—Citrate	20	70	100	126	70	4.03	20,950	92	4	1	1	2	50	63
	Oxalate	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
	Heparin	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
J. B., a boy, aged 3 months; fibroblastic tumor under chin (malignant); duration, 1½ months; ulceration on surface; 3/26/28, excised	Citrate	3	10	23	86	60	3.83	9,650	30	40	27	2	1	11.5	43
	Oxalate	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
	Heparin	..	..	...	...	..	....	.....	..	..	..	..	..	....	....

TABLE 10.—*Sedimentation Rate in Meningitis*

	Readings in Mm.	Sedimentation in Hours ½	1	2	24	Hemoglobin, per Cent	Red Blood Cells in Millions	White Blood Cells	Differential: Polymorphonuclears	Small Lymphocytes	Large Lymphocytes	Large Mononuclears	Transitionals	Plasma, per Cent by Volume: 2 Hours	24 Hours
V. B., a girl, aged 4 years; meningococcus meningitis; duration, 1 week; antimeningococci serum given; temperature, 99 on 3/14/28; recovery; discharge, 3/29	3/14—Citrate	50	77	97	120	83	4.96	15,050	..	..	..	..	..	48.5	60
	Oxalate	90	100	107	114	..	....	.....	..	..	..	..	..	53.5	57
	Heparin	84	93	96	125	..	....	.....	..	..	..	..	..	48	62.5
G. J., a girl, aged 8 years; meningococcus meningitis; duration, 2 weeks; antimeningococci serum given; temperature, 99.2 on 1/7/28; recovered 1/25/28	1/ 7—Citrate	4	11	25	86	88	4.77	11,400	36	22	42	..	..	13.5	43
	Oxalate	3	7	26	88	..	....	.....	..	..	..	..	..	13	44
	Heparin	8	24	48	115	..	....	.....	..	..	..	.	..	24	57.5
G. R., a boy, aged 2 years; meningococcus meningitis; duration, 11 days; temperature, 99; unconscious on 3/16/28; artimeningococci serum given; May 4, recovered	3/16—Citrate	1	3	5	77	50	4.82	11,700	..	..	..	..	..	2.5	38.5
	Oxalate	10	25	60	104	..	....	.....	..	..	..	..	..	30	52
	Heparin	5	20	52	116	..	....	.....	..	..	..	..	..	36	58
	3/30—Citrate	20	62	87	127	..	....	16,900	..	..	..	..	..	43.5	68.5
	Oxalate	18	76	107	125	..	....	.....	..	..	..	..	..	53.5	62.5
	Heparin	10	80	109	121	..	....	.....	..	..	.	..	..	54.5	60.5
A. G., a girl, aged 9 years; chronic meningococcus meningitis; duration, 2 months; temperature, 99 on 3/13/28; on milk diet; condition poor; died, 3/23/28	3/13—Citrate	23	71	98	110	80	5.33	16,000	..	.	..	..	..	49	55
	Oxalate	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
	Heparin	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
H. B., a girl, aged 4 years; upper respiratory infection; duration, 2 days; meningismus; spinal fluid normal; temperature, 100 on 4/7/28; recovered	4/ 7—Citrate	3	8	16	33	..	....	11,650	69	20	10	..	..	8	16.5
	Oxalate	5	11	42	69	..	....	.....	..	..	..	..	..	21	34.5
	Heparin	6	22	61	100	..	....	.....	..	..	..	..	..	30.5	50

TABLE 11.—*Sedimentation Rate in Choreas*

	Readings in Mm.	Sedimentation in Hours ½	1	2	24	Hemoglobin, per Cent	Red Blood Cells in Millions	White Blood Cells	Differential: Polymorphonuclears	Small Lymphocytes	Large Lymphocytes	Large Mononuclears	Transitionals	Plasma, per Cent by Volume: 2 Hours	24 Hours
G. G., a boy, aged 13 years; acute chorea; endocarditis; duration, 8 weeks; temperature, 101; chorea severe	2/28/28—Citrate	35	105	120	126	60	4.72	17,750	71	18	4	6	..	60	63
	Oxalate	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
	Heparin	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
Temperature, 100; condition severe	3/ 1/28—Citrate	15	45	75	108	67	4.47	23,000	77	17	6	..	..	37.5	54
	Oxalate	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
	Heparin	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
Temperature, 98.8; slight improvement	3/ 5/28—Citrate	11	34	55	132	..	....	19,980	..	.	.	.	..	27.5	66
	Oxalate	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
	Heparin	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
Throat infection; improvement in chorea	3/13/28—Citrate	25	86	130	140	..	....	18,850	..	.	..	..	..	65	70
	Oxalate	40	60	131	132	..	....	.....	..	..	..	.	..	65.5	66
	Heparin	12	115	115	120	..	....	.....	..	..	.	.	..	57.5	60
Temperature, 99; condition good	3/16/28—Citrate	38	70	112	140	..	....	.....	..	..	..	.	..	56	70
	Oxalate	69	101	129	140	..	....	.....	.	.	..	..	..	64.5	70
	Heparin	90	111	117	121	..	....	.....	..	.	..	..	..	58.5	60.5
Temperature, 98.8; throat improved	3/21/28—Citrate	38	74	116	138	..	....	18,500	..	.	..	..	..	58	69
	Oxalate	42	93	130	136	..	....	.....	..	.	.	..	..	65	68
	Heparin	..	..	83	120	..	....	.....	..	..	.	..	..	41.5	60
Temperature, 98.8; improved	3/24/28—Citrate	20	77	94	131	59	4.01	13,900	..	..	..	..	..	47	65.5
	Oxalate	40	120	123	128	..	....	.....	.	..	..	..	..	61.5	64
	Heparin	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
Condition good	3/28/28—Citrate	..	100	140	145	..	....	.....	..	..	..	..	..	70	72.5
	Oxalate	65	117	125	132	..	....	.....	..	..	.	..	..	62.5	66
	Heparin	40	114	120	127	..	....	.....	..	..	.	.	..	60	63.5
Temperature, 98.8	4/ 4/28—Citrate	53	80	107	125	..	....	12,250	..	.	..	..	..	53.5	62.5
	Oxalate	80	110	118	125	..	....	.....	..	..	..	..	..	59	62.5
	Heparin	43	93	110	115	..	....	.....	..	.	..	..	..	55	57.5
Temperature, 98.6	4/11/28—Citrate	20	71	95	122	..	...	13,450	..	..	..	.	..	47.5	61
	Oxalate	25	55	105	120	..	....	.....	..	.	.	..	..	52.5	60
	Heparin	15	92	112	118	..	....	.....	..	.	..	.	..	56	59
Temperature, 99	4/16/28—Citrate	1	2	7	70	..	....	13,850	..	..	..	..	..	3.5	35
	Oxalate	12	29	60	95	..	....	.....	..	..	..	..	..	30	47.5
	Heparin	3	65	108	115	..	....	.....	..	..	..	.	..	54	57.5
Temperature, 99; recovered	4/23/28—Citrate	16	32	70	120	..	....	14,890	..	..	.	..	..	35	60
	Oxalate	11	29	55	100	..	....	.....	..	..	..	..	..	27.5	50
	Heparin	14	30	103	108	..	....	.....	..	..	..	.	..	51.5	54

TABLE 12.—*Sedimentation Rate in Scarlatina*

	Readings in Mm.	Sedimentation in Hours ½	1	2	24	Hemoglobin, per Cent	Red Blood Cells in Millions	White Blood Cells	Differential: Polymorphonuclears	Small Lymphocytes	Large Lymphocytes	Large Mononuclears	Transitionals	Plasma, per Cent by Volume: 2 Hours	24 Hours
P. F., a boy, aged 6 years; scarlet fever; duration, 1 day; temperature, 102.6; on admission, 12 cc. of scarlet fever antitoxin was given; 3/26/28, rash fading; cervical adenitis serum; temperature, 101 on 3/30/28; peeling; irregular temperature for 5 days, at times as high as 103; 4/11/28, temperature, 99; 4/13/28, erythema nodosum; otitis media on the right; 4/16/28, temperature, 101, continues irregular; 4/21/28, blood sugar, 114 mg.; recovered	3/24—Citrate	3	74	90	110	85	5.59	15,750	..	..	..	..	..	45	55
	Oxalate	50	65	83	100	..	....	.....	..	..	..	..	..	41.5	50
	Heparin	25	46	71	96	..	....	.....	..	..	..	..	..	35.5	48
	3/25—Citrate	3	6	16	70	..	....	8,000	..	..	..	..	..	8	35
	Oxalate	6	12	25	95	..	....	.....	..	..	..	..	..	13	47.5
	Heparin	6	15	33	122	..	....	.....	..	..	..	..	..	16.5	61
	3/30—Citrate	15	53	68	83	..	....	.....	..	..	..	..	..	34	41.5
	Oxalate	18	76	95	115	..	....	.....	..	..	..	..	..	47.5	57.5
	Heparin	88	101	105	120	..	....	.....	..	..	..	..	..	52.5	60
	4/ 2—Citrate	17	33	44	73	..	....	.....	..	..	..	..	..	22	36.5
	Oxalate	25	55	74	86	..	....	.....	..	..	..	..	..	37	43
	Heparin	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
	4/11—Citrate	10	45	118	140	..	....	10,000	..	..	..	..	..	59	70
	Oxalate	63	95	120	130	..	....	.....	..	..	..	..	..	60	65
	Heparin	26	83	110	118	..	....	.....	..	..	..	..	..	55	59
	4/16—Citrate	105	120	130	142	..	....	12,900	..	..	..	..	..	65	71
	Oxalate	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
	Heparin	..	..	...	...	..	....	.....	..	..	..	..	..	....	....
E. A., a boy, aged 8 years; arthritis of hip; (scarlet fever 2 weeks previously); duration, 2 days; 4/7/28, temperature, 100.4; recovery, 4/21/28	4/ 7—Citrate	50	85	106	115	..	....	14,850	68	..	20	2	..	53	57.5
	Oxalate	95	118	124	125	..	....	.....	..	..	..	..	..	62	62.5
	Heparin	22	59	103	115	..	....	.....	..	..	..	..	..	51.5	57.5
C. X., a girl, aged 8 years; scarlet fever; duration, 4 days; 3/16/28, temperature normal; recovery	3/16—Citrate	4	25	56	93	85	5.02	12,520	83	11	5	1	..	28	46.5
	Oxalate	10	50	79	107	..	....	.....	..	..	..	..	..	39.5	53.5
	Heparin	5	53	88	104	..	....	.....	..	..	..	..	..	44	52

CONCLUSIONS

In our experience with the sedimentation rate, we hesitate to advise its general use to the practicing physician. We believe that:

1. One determination of the rate is of little value in diagnosis and of no value in prognosis.

2. A single normal or slightly increased or decreased rate means little. A single rapid rate indicates some abnormality.

3. If, in attempting to define the limits of normal, one allows sufficient latitude to include the commonly observed variation, many pathologic conditions will also fall within the limits.

4. The variations between the various anticoagulants are difficult for us to interpret. They do not parallel any other observations.

5. Frequent leukocyte and differential counts have been of much more assistance in following the clinical course of disease than have frequent sedimentation readings.

6. The sedimentation rate does not seem to indicate the degree of resistance to disease or the extent of the lesion in most of our cases.

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ABSTRACT OF DISCUSSION

DR. S. J. SEEGER: This work was undertaken because of the enthusiasm with which this test was hailed by many physicians who had applied it to clinical medicine. We had hoped that we would be able to adapt it to our work at the Milwaukee Children's Hospital. However, a study of the material which Dr. Peterman has partially presented brings out some interesting points. If we leave out of consideration the variations which one finds in using different technics, the amount of blood and so on, there are other factors which also influence this test and in that way affects its reliability. Dr. Peterman has illustrated the great variations which are a result of the use of various anticoagulants. The dilution factor enters in when citrate is used, and the electrolyte factor is of importance when oxalates are used. Other factors, such as the time that elapses after the blood is taken and conditions under which the blood is withdrawn, also exert inconstant and irregular influences on the reading. To these irregularities the variations in the rate, as demonstrated in normal persons, are added, and it becomes obvious that the evaluation of the sedimentation rate becomes conflicting and confusing. One must allow a wide variation in the normal and in this way include persons who are suffering from fatal disease, or the normal limits must be restricted. In this way the accuracy and sensitiveness of the test are sacrificed. The cases which Dr. Peterman has tabulated are largely self explanatory. In all but exceptional cases, we have found that the leukocyte count and the differential blood counts which are much more easily made have been of far greater value in diagnosis and prognosis. They have offered a more comprehensive guide as to the progress of our cases, whereas frequent sedimentation rates offered us little aid in most instances.

In certain cases in which other routine laboratory data are available, we feel that the sedimentation rate may offer additional support but, on the other hand, when all other examinations give negative results, a search is made for the extreme. Oxalate powders, in their effect on normal as well as on pathologic bloods, have not been satisfactorily interpreted, and, suffice it to say, the twenty-four hour reading does not parallel the cell volume nor do the earlier readings parallel the clinical course. It is probable that we have not exhausted the possibility of value in the interpretation of our data.

This test has limited use from a diagnostic standpoint, and we do not agree with those men who feel that these readings can be interpreted as paralleling the defensive mechanism of the organism in acute infection disease.

EXPERIMENTAL WHOOPING COUGH *

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Within two years after Bordet and Gengou [1] had grown their gram-negative, influenza-like bacillus on a special potato-blood-agar medium, Klimenko [2] claimed to have produced whooping cough easily in four monkeys and ninety-six puppies by inoculation and by transmission from one animal to another. In 1912, Mallory, Hornor and Henderson [3] dropped cultures into the nares of rabbits, puppies and three *Rhesus* monkeys. The monkeys remained well, but the rabbits became emaciated and developed signs of snuffles. A gram-negative bacillus was grown from the nares and trachea of the infected animals. Histologic studies revealed numerous gram-negative bacilli between the cilia of the trachea and larynx. The conclusion was that the experiments "supplied the steps which have heretofore been lacking, according to Koch's laws, for the complete demonstration that the Bordet-Gengou bacillus is the cause of whooping cough." In tests with dogs suffering from distemper, Galli and Valerio,[4] in 1908, isolated a bacillus which they considered the cause of the disease. Ferry [5] and others produced subsequent proof that distemper in dogs and cats and snuffles in rabbits and guinea-pigs are caused by *Bacillus bronchisepticus* and *Bacillus lepisepticum*. These influenza-like, gram-negative bacilli grow readily in blood-free culture mediums. M'Gowan [6] and Ferry isolated *B. bronchisepticus* a number of times from the respiratory tract of monkeys, also from a man with a severe cough. Rhea [7] found a lesion in dogs with distemper which resembled that described by Mallory in experimental pertussis; he found similar lesions in rabbits with snuffles. Theobald Smith's [8] study of the lesion in guinea-pigs infected with *B. bronchisepticus* led him to conclude that: "This

* Submitted for publication, Sept. 18, 1928.

* From the Laboratories of the Evanston Hospital.

1. Bordet, J., and Gengou, O.: Ann. de l'Inst. Pasteur **20**:731, 1906.
2. Klimenko, W.: Centralbl. f. Bakteriol. **46**:218, 1908.
3. Mallory; Hornor, and Henderson: J. M. Research **27**:115, 1913; **27**:391, 1912.
4. Galli and Valerio: Centralbl. f. Bakteriol. **41**:103, 1908.
5. Ferry, N.: J. Infect. Dis. **8**:399, 1911.
6. M'Gowan, J.: J. Path. & Bact. **15**:372, 1911.
7. Rhea, L.: J. M. Research **32**:471, 1915.
8. Smith, T.: J. M. Research **29**:291, 1913.

and other evidence makes it highly probable that the bacillus found by Mallory in the respiratory tract of animals treated with *B. pertussis* of Bordet was *B. bronchisepticus.*" Brown [9] recently found *B. bronchisepticus* in a child with a severe, paroxysmal cough which resembled whooping cough. The child had played with a pet rabbit which had typical snuffles. No blood counts were reported, but the bacillus was isolated from the child and from the nares of the rabbit. Agglutination tests were positive for *B. bronchisepticus.* Arnheim,[10] Manicatide,[11] Fraenkel,[12] Melfi,[13] Poleff,[14] and Bachmann and Burghard [15] failed to produce typical pertussis in monkeys, puppies or rabbits. In 1924, Jochmann [16] said:

> It is questionable whether clinical pertussis can be produced in animals. The causative organism of pertussis is not yet definitely determined. The Bordet-Gengou bacillus is, at present, considered the presumable cause because it is the only one of the influenza-like bacilli in which, with the aid of serological methods (agglutination and complement fixation), one can prove a close biological relation to the serum of pertussis convalescents.

In 1912, Inaba,[17] in Japan, failed to produce symptoms of pertussis in puppies, but produced a severe paroxysmal cough in a red-faced *Macacus* monkey, aged 10 months, within two weeks after a freshly isolated, forty-eight hour growth of *B. pertussis* had been swabbed on the pharynx. From five to ten short coughs occurred in close succession. Seventeen days after inoculation there were several severe paroxysms which ended with expectoration of mucus and vomiting of food. The paroxysms resembled those of pertussis in human beings without the inspiratory whoop. A gram-negative bacillus was recovered from mucus on the pharynx and from vomited mucus, but it was not described as hemoglobinophilic. The cough gradually subsided, the appetite improved and the complement-fixation test was positive. The work of Inaba did not include white cell and differential blood counts, cultures before the inoculation (to exclude distemper bacilli), nor was there a preliminary complement-fixation test. Bachmann and Burghardt maintained that Inaba alone produced unquestionable experimental pertussis. Reference has not been made in any work on experimental whooping cough to the increase in the white cell count and the prepon-

9. Brown, J.: Bull. Johns Hopkins Hosp. **38**:147, 1926.
10. Arnheim, G.: Arch. f. Kinderh. **50**:296, 1909.
11. Manicatide, M.: Ztschr. f. Kinderh. **7**:226, 1913.
12. Fraenkel, C.: München. med. Wchnschr. **55**:1683, 1908.
13. Melfi, J.: Semana méd. **30**:1125, 1923.
14. Poleff, L.: Centralbl. f. Bakteriol. **69**:23, 1909.
15. Bachmann, W., and Burghard, E.: Ztschr. f. Kinderh. **39**:465, 1925.
16. Jochmann, G.: Lehrbuch der Infektionskrankheiten, Berlin, Julius Springer, 1924.
17. Inaba, I.: Ztschr. f. Kinderh. **4**:252, 1912.

derance of lymphocytes in the differential count, two laboratory tests long regarded as significant in the diagnosis of this disease.

The following report deals with repeated attempts to produce experimental whooping cough in twenty-eight young, apparently healthy monkeys, ten of them, *Macacus rhesus* and eighteen of the genus *Cebus*, called "ringtail." The thirty-two strains of Bordet-Gengou bacilli used in the tests included a strain obtained from Professor Bordet, six strains from Dr. Povitzky of the New York Bureau of Laboratories, and twenty-five strains freshly isolated by the cough plate method of Chievitz and Meyer [18] from early cases of pertussis. In seventeen tests, twenty-four to forty-eight hour surface growths suspended in a physiologic solution of sodium chloride were swabbed on the pharynx and dropped into the eyes and nose of the animal; on eight occasions, animals were intimately exposed to children who were in the paroxysmal stage of the disease, or freshly coughed up mucus was swabbed into the nose and throat. In twenty-one tests, the suspension was dropped into the nares after a slight asphyxia had been produced by pressure on the mouth and nose. In thirty tests, saline suspensions were injected through the ventral wall of the larynx; when the needle was directed downward, part of the culture reached the trachea. Eight of the seventy-six tests were followed, in from seven to twenty days, by coughs which usually became paroxysmal. Besides other control tests, injections were repeated on some of the animals that had recovered from the cough, but with negative results; the animals had acquired an immunity to the bacillus. The characteristic changes in the white cell and differential blood counts were detected only when the cough was present. The animals were kept under preliminary observation, usually for a week or longer, to insure a good state of health. The work during this period included white cell and differential blood counts, rectal temperatures, hemoglobin determinations and cultures of throat mucus made on plates of Bordet medium. Distemper bacilli (*B. bronchisepticus* or *B. lepisepticum*) were not found in any instance. Various diagnostic tuberculin tests, made in the first series of animals, invariably gave negative results and were discontinued. When an animal was used for more than one inoculation, ample time was usually allowed to elapse between tests. Most of the animals were under observation for months, some for over a year. Except in the tests for transmission of the disease from animal to animal, the monkeys tested were kept in separate cages. Preliminary leukocyte counts often revealed surprising daily variations. The fluctuations were less pronounced in the differential counts. The preliminary leukocyte counts of the *Macacus* monkeys were more variable

18. Chievitz, J., and Meyer, A.: Arch. f. Kinderh. **66**:186, 1918.

and the average was usually higher than those of the ringtail monkeys. Each animal seemed to have its individual range of fluctuation; that is, if the preliminary leukocyte count was low it seldom exceeded 7,000 cells per cubic millimeter; if it was high it usually averaged between 14,000 and 20,000 cells per cubic millimeter. To eliminate as many factors as possible, the blood was usually taken from visible skin veins of the ears in the morning before feeding, and individual blood pipets

Inoculation of Eight Monkeys with B. Pertussis

			Differential Counts						
Experiment	Time	Average White Cell Count	Polymorphonuclears	Lymphocytes	Eosinophils	Transitionals	Large Mononuclears	Basophils	Comment
Klieneberger*	.....	7,470	35.8	58	3.4	1.2	1.3	0.3	Various genera
Monkey 1....	Before	7,350	35.0	61	2.0	2.0	...	...	Paroxysmal cough for 3 weeks
	During	14,100	25.0	73	...	...	2.0	...	
	After	8,830	36.0	62	...	...	2.0	...	
Monkey 2....	Before	9,100	....	..	...	...	...	...	Paroxysmal cough; killed; three small lesions in larynx
	During	21,250	8.0	89	3.0	...	...	...	
	After	13,250	14.0	85	...	...	...	1.0	
Monkey 3....	Before	15,000	68.0	31	...	1.0	...	...	Cough for 10 days; found dead; colitis; recovered B. pertussis 17 days after injection
	During	21,500	17.0	74	9.0	...	...	...	
Monkey 4....	Before	14,600	32.0	67	...	1.0	...	...	Coughed for a month; subsequently immune to six intralaryngeal injections
	During	27,566	28.0	68	...	1.0	2.0	1.0	
	After	15,645	31.0	67	...	2.0	...	...	
Monkey 5....	Before	20,700	78.0	22	...	...	...	...	Killed; lesions in larynx; recovered B. pertussis from lesion
	During	27,150	45.0	50	2.0	2.0	...	1.0	
Monkey 6....	Before	18,429	50.0	46	3.0	1.0	...	...	Coughed for 3 weeks; subsequently immune
	During	39,500	29.0	67	...	4.0	...	...	
	After	17,700	44.0	56	...	...	...	...	
Monkey 7....	Before	16,837	48.0	44	8.0	...	...	...	Killed; recovered B. pertussis from both lungs
	During	62,800	32.0	68	...	...	...	...	
Monkey 8....	Before	14,050	48.0	50	2.0	...	...	...	Killed; recovered B. pertussis from tracheal wall
	During	24,000	57.0	41	2.0	...	...	...	

* Normal blood counts reported by Carl Klieneberger in "Die Blutmorphologie der Laboratoriumstiere," Leipzig, Barth, 1927.

were used for each animal. Average leukocyte counts were usually established for the animals before they were inoculated, during the first week of the cough, and after the cough had ceased. The table and charts were prepared from the protocols of the animals that coughed after the injections of *Bacillus pertussis*; control animals that failed to cough after inoculations and animals reinjected after recovery from the cough did not show these changes. In animals that died of intercurrent bronchopneumonia or enteritis, a neutrophilic leukocytosis was found.

As several of the animals that developed paroxysmal coughs and lymphocytosis had previously received injections of other strains without effect, the virulence of various strains was tested in white mice. As a rule, 0.5 cc. of a fresh saline suspension containing from one to two billion pertussis bacilli per cubic centimeter was injected intraperitoneally. Six of fifteen recently isolated strains proved fatal within forty-eight hours. After several months, this virulence was lost; that is, similar and larger doses of two day cultures were no longer fatal for mice when injected intraperitoneally. The culture obtained from Professor Bordet, the six New York strains, and old strains which had been isolated from patients, months previously, were not fatal in the forementioned dose. Autopsies performed soon after death usually revealed hyperemia of the parietal peritoneum, with the greatest intensity at the site of the injection. Smears of the cherry colored peritoneal fluid showed leukocytes, but pertussis bacilli could not be found. Cultures of this fluid in one instance were negative, otherwise *B. pertussis* was recovered in pure culture. Pertussis bacilli were recovered once only in cultures made of blood from the heart.

Five recently isolated strains of *B. pertussis* injected intraperitoneally into guinea-pigs were fatal in a dose of 1 cc. or more (about one billion bacilli per cubic centimeter); animals which received less than 0.5 cc. did not die. Five-tenths cubic centimeter of a strain under cultivation for nine months was not fatal. Observations made at autopsy coincided with those given by Bordet: The parietal and visceral peritonea were extremely hyperemic, and cherry colored fluid was abundant in the peritoneal cavity. The fluid contained many leukocytes, but the presence of *B. pertussis* could not be demonstrated in smears. Cultures of this fluid and of the blood of the heart invariably were negative.

PROCEDURE

In the first series, forty-eight hour surface growths, suspended in a physiologic sodium chloride solution, were sprayed in the immediate vicinity of the animals. A few weeks later, similar suspensions were dropped into the eyes and nose, swabbed on the pharynx or injected into the antrums. All these tests were unsuccessful. Two animals (monkeys 1 and 2) which resisted such inoculations received injections intralaryngeally. Nine days later, both animals began to cough. The paroxysms soon increased in frequency and severity. On several occasions, mucus and food were vomited after coughing. Lymphocytosis was present in both animals and severe paroxysms continued for weeks. The cough then gradually subsided.

Monkey 1.—Ringtail monkey, male, arrived on Dec. 5, 1925; weight, 1,700 Gm.; hemoglobin, 70 per cent; average of 7 daily leukocyte counts, 7,350 per cubic millimeter.

December 11: Dropped 2 cc. of forty-eight hour culture, strain "Jean H.," into eyes, nose and mouth; no cough or change in white cell count.

Jan. 2, 1926: Exposed for one and a half hours to a child in the third paroxysmal week of whooping cough; also swabbed fresh mucus into the nose; no cough, no increase in leukocyte count.

January 25: Injected 2 cc. of a three day growth of *B. pertussis* into larynx and trachea (chart 1).

February 2: First cough.

February 3: Cough more frequent; polymorphonuclears, 35; lymphocytes, 61; transitionals, 2; basophils, 2.

February 4: Cough more severe; five hacks in one paroxysm.

February 5: Cough still more frequent.

February 6: First paroxysm.

February 8: Typical paroxysms; weight, 1,560 Gm.; leukocytes, 19,880; differential count: polymorphonuclears, 25; lymphocytes, 69; large mononuclears, 4; transitionals, 2.

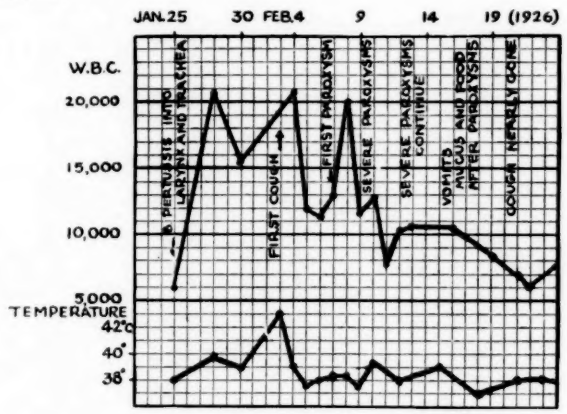

Chart 1 (monkey 1).—Leukocytosis following the intratracheal injection of Bacillus pertussis.

February 9: Coughed sixteen times.

February 10: Coughed sixteen times; seventeen hacks in one paroxysm; vomited mucus and food after paryoxysms.

February 15: Cough less frequent; still vomits mucus after severe cough.

February 18: Cough less severe; polymorphonuclears, 36; lymphocytes, 62; large mononuclears, 2.

February 22: A few spontaneous coughs.

February 26: Seldom coughed.

March 2: Coughed infrequently.

Monkey 2.—Ringtail monkey, male, arrived on Dec. 11, 1925; weight, 2,000 Gm.; hemoglobin, 75 per cent.

Dec. 11, 1925, to Jan. 11, 1926: Average leukocyte count, 9,100 per cubic millimeter.

January 12: Swabbed nose and throat with strain "Ventriss"; also dropped some into nose; no cough; no increase in leukocytes (chart 2).

January 25: Injected 2 cc. of a three day growth of *B. pertussis* into larynx and trachea.

February 2: First cough; frequent sneezing and profuse rhinitis.

February 3: Cough more frequent; polymorphonuclears, 8; small lymphocytes, 78; large lymphocytes, 11.

February 4: Cough more severe and more frequent; eleven hacks in one paroxysm.

February 5: Frequent paroxysms; sixteen hacks in one paroxysm.

February 5: Frequent paroxysms; sixteen hacks in one paroxysm.

February 8: Polymorphonuclears, 14; small lymphocytes, 73; large lymphocytes, 12; basophils, 1.

February 10: Twenty-six hacks in a paroxysm; mucus and food vomited after severe paroxysms.

February 11: Cough continued; vomited after severe cough.

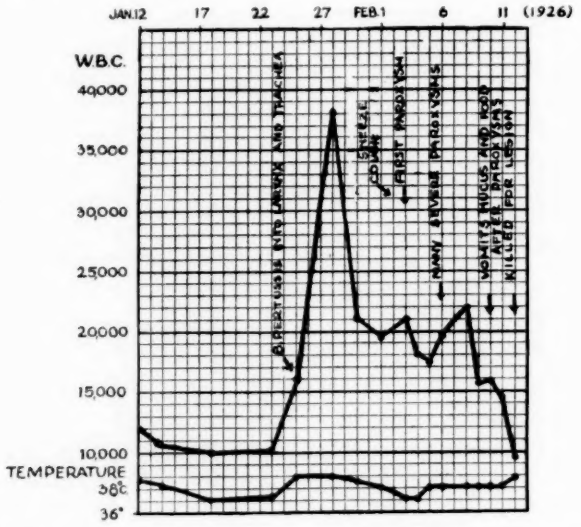

Chart 2 (monkey 2).—Marked leukocytosis following the intratracheal injection of B. pertussis.

February 13: Killed by injection of air into heart. At autopsy soon after death, the epiglottis and glottis were found a pale pearly white. On the inner surface of the glottis there were three bright red, hemorrhagic areas, 4 by 2 mm., 2 by 2 mm. and 3 by 2 mm., respectively, with much tenacious mucus in the vicinity. Smears contained leukocytes and gram-negative bacilli in abundance. Except for a number of minute superficial hemorrhagic spots on the tracheal wall just below the larynx, the trachea was pale, smooth and shiny. The lymph glands in this region were not enlarged; the lungs and other organs appeared normal.

Monkey 3.—Ringtail monkey, male, arrived Feb. 17, 1926; weight, 1,240 Gm.; hemoglobin, 65 per cent.

February 17: Leukocytes, 14,150; polymorphonuclears, 68; small lymphocytes, 16; large lymphocytes, 15; transitionals, 1; caged for four weeks with

monkey 1, which had been coughing for fifteen days; the white cell and differential blood counts remained fairly constant; no cough.

March 18: Leukocytes, 12,300; polymorphonuclears, 55; small lymphocytes, 31; large lymphocytes, 13; large mononuclears, 1.

March 31: Injected 1 cc. of the strain "Bell" into larynx and trachea.

April 12: Injected 2 cc. of a heavy emulsion of the strain "Bell" into larynx and trachea (chart 3).

April 16: First cough.

April 19: Coughed five times in an hour; leukocytes, 26,750; polymorphonuclears, 17; small lymphocytes, 60; large lymphocytes, 14; eosinophils, 9.

April 21: Negative results from deep throat culture.

April 23: Cough continued.

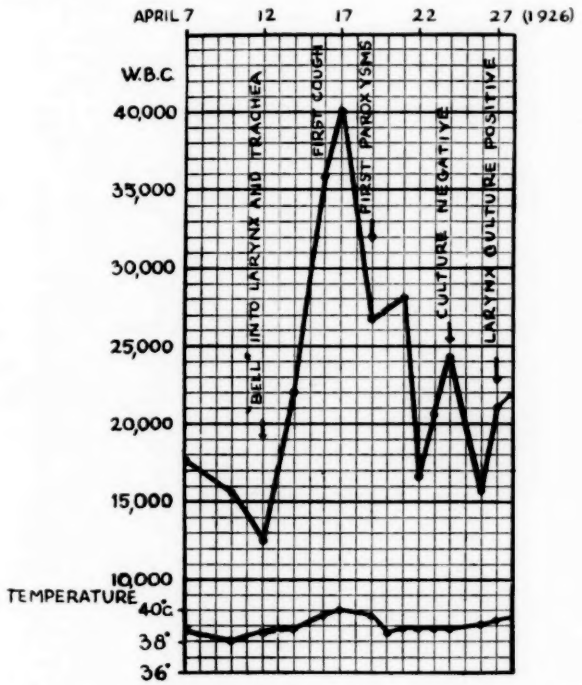

Chart 3 (monkey 3).—Marked transient leukocytosis during the period of coughing.

April 27: Less cough; enteritis.

April 29: Found dead; autopsy revealed hemorrhagic colitis; ulcers in colon; absence of visible hemorrhage or lesion in larynx or trachea; lungs appeared normal. There were several ulcers in the small and large bowel. Culture of mucus taken from the larynx showed more than fifty typical colonies of *B. pertussis*, at the end of four days. Cultures of blood from the heart did not disclose pertussis bacilli.

Monkey 4.—Ringtail monkey, male, arrived on May 13, 1926; weight, 600 Gm.; hemoglobin, 70 per cent.

May 17: Injected 2 cc. of a five day growth of the strain "Eddy," into larynx and trachea (chart 4).

June 2: Average leukocyte count for the previous two weeks, 14,600.

June 3: Sneezed six times in one hour.

June 4: First cough.

June 7: Cough more severe.

June 8: Cough more frequent.

June 9: Deep throat culture gave positive results.

June 12: Antrums aspirated; growth not found; deep throat cultures showed *B. pertussis.*

June 14: Coughed nine times in an hour; five hacks in one paroxysm.

June 19: Cough less severe and less frequent.

June 26: Seldom coughed.

August 6: Injected a mixture of six strains into larynx and trachea.

October 10: No cough since the end of June; leukocyte counts varied between 7,000 and 15,000 cells per cubic millimeter.

October 17: Injected 1 cc. of strain "Courshon" into larynx and trachea.

November 9: No cough since June; injected 1 cc. of a three day growth of strain "Eddy" into larynx and trachea.

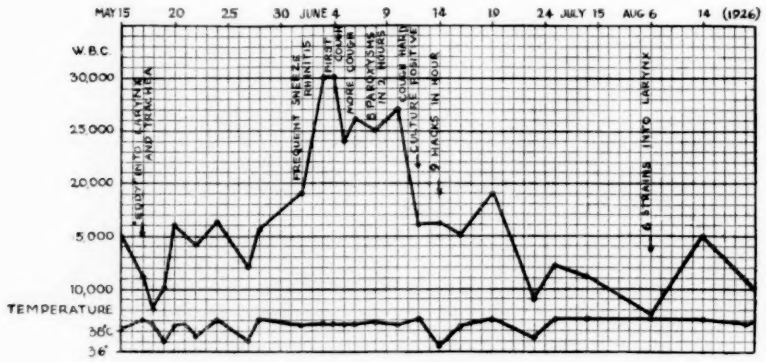

Chart 4 (monkey 4).—Leukocytosis following the injection of B. pertussis. The culture was positive for B. pertussis during the paroxysmal stage.

December 22: No cough; injected a mixture of twelve strains into larynx and trachea.

March 21, 1927: No cough; dropped 1 cc. of a three day growth of strain "Smith" into nose and throat.

April 13: Killed; at autopsy, hemorrhage or lesion was not found in the larynx, trachea or lung; smears and cultures gave negative results; blood taken from the heart did not show *B. pertussis.* Repeated injections had not left a trace in the wall of the larynx.

Monkey 5.—Ringtail monkey, male, arrived on Jan. 13, 1927; weight, 960 Gm.

January 14: Leukocytes, 20,700; polymorphonuclears, 78; small lymphocytes, 19; large lymphocytes, 3; injected 1 cc. of strain "Eddy" into larynx and trachea.

February 8: First cough.

February 9: Pressure on larynx produced paroxysms; leukocytes, 20,600; polymorphonuclears, 42; small lymphocytes, 56; large lymphocytes, 1; transitionals, 1.

February 10: Spontaneous paroxysm but not as severe as when larynx was compressed; leukocytes, 27,150; polymorphonuclears, 45; lymphocytes, 50; transitionals, 2; eosinophils, 2; basophils, 1.

February 15: Paroxysms longer, consisting of six or more hacks in close succession; deep throat culture negative.

February 19: Cough-plate exposed during paroxysm gave negative results.

March 5: Longer paroxysms when throat was compressed.

March 10: Still coughed in paroxysms; ate well.

March 12: Still coughed in paroxysms; anesthetized; at autopsy, several minute hemorrhagic areas found on the inner surface of the larynx. The largest measured 2 by 2 mm. and was located to the left of the midline, the possible site of the needle prick; it was 8 mm. below the upper margin of the vocal cord. The lesion could not be removed; cultures made from it were positive for *B. pertussis*. With a hand lens, similar but smaller submucous, bright red areas were seen on the flesh-colored folds of the vocal cords, about midway between the upper margin of the vocal cord and the large lesion. Cultures of laryngeal and tracheal mucus were negative. Six similar but more minute hemorrhagic areas were found in the tracheal wall at the first ring of cartilage; cultures on a Bordet plate did not show a growth. The lungs and other organs were apparently normal. The larynx was sectioned (15 microns), and stained with hematoxylin-eosin, but pertussis bacilli could not be found.

After paroxysmal coughs with lymphocytosis had been produced in these five young ringtail monkeys by the injection of various strains of *B. pertussis* into the larynx and trachea, it was decided to use a technic which would not require traumatization. As tests with spray, swab and aspiration did not produce a cough, the following method was evolved: A slight degree of asphyxia was produced by compression of the mouth and nose; then one nostril was released and simultaneously the saline suspension of *B. pertussis* was dropped in. This was repeated until from 1 to 2 cc. of the liquid was drawn into the deeper parts of the respiratory tract. A summary of three such tests follows:

Monkey 6.—*Macacus rhesus* monkey, male, arrived on Sept. 3, 1927; weight, 1,680 Gm.; hemoglobin, 80 per cent.

October 1: Average leukocytes for September, 18,429; polymorphonuclears, 50; lymphocytes, 46; eosinophils, 3; transitionals, 1. Dropped 1.5 cc. of a four day growth of strain "Pearson" into nares, by the method described (chart 5).

October 3: Dropped 1.5 cc. two-day growth, strain "Pearson" into nares.

October 10: Polymorphonuclears, 50; small lymphocytes, 41; large lymphocytes, 4; eosinophils, 5. Watery rhinitis; *B. pertussis* recovered from cultures from nose and throat; also found in smears.

October 13: First cough.

October 14: Cough more frequent.

October 17: Coughed four times while eating sugar.

October 21: Coughed five times in an hour; polymorphonuclears, 29; lymphocytes, 67; transitionals, 4.

November 18: No cough during the past few weeks; dropped 1 cc. of the strain "Webber" into nares; polymorphonuclears, 36; small lymphocytes, 50; large lymphocytes, 12; transitionals, 1; eosinphils, 1; cough did not follow; average leukocyte count from November to January, 17,500.

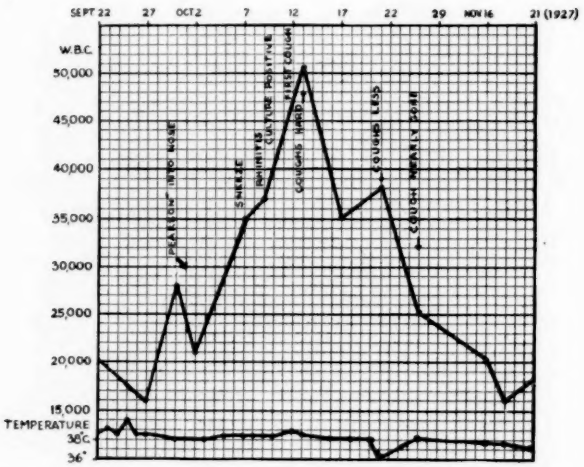

Chart 5 (monkey 6).—Marked leukocytosis following the inoculation of B. pertussis into the nares. B. pertussis was recovered from nose and throat. Leukocytosis did not follow subsequent injections.

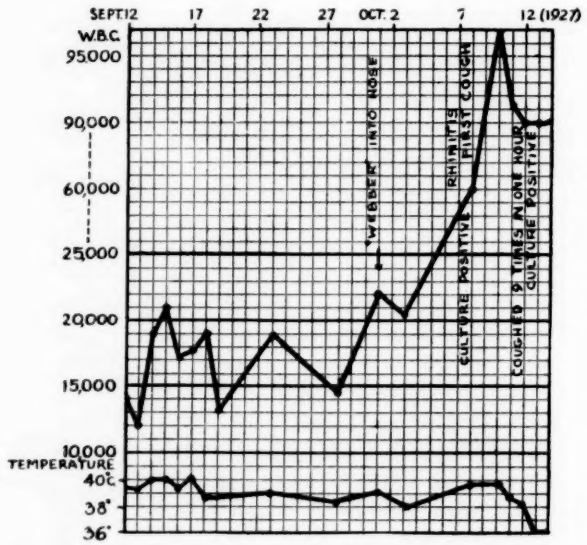

Chart 6 (monkey 7).—Marked leukocytosis, reaching 97,000. B. pertussis was recovered from the lung.

Feb. 16, 1928: Dropped 2 cc. five-day growth, strain "Ochs" into nares; polymorphonuclears, 41; small lymphocytes, 50; large lymphocytes, 9.

February 29: Leukocytes, 11,750; polymorphonuclears, 44; small lymphocytes, 52; large lymphocytes, 4; has not coughed since October (immune).

Monkey 7.—*Macacus rhesus* monkey, male, arrived on Sept. 10, 1927; weight, 1,600 Gm.; hemoglobin, 80 per cent.

September 12 to 28: Average leukocyte count, 16,837; polymorphonuclears, 48; small lymphocytes, 29; large lymphocytes, 15; eosinphils, 8 (chart 6).

October 1: Dropped 1.5 cc. two-day growth of the strain "Webber" into nares.

October 7: Leukocytes, 59,750; polymorphonuclears, 32; small lymphocytes, 57; large lymphocytes, 11; rhinitis.

October 8: First cough.

October 10: Profuse rhinitis; culture from nose shows *B. pertussis.*

October 11: Coughed more; appeared ill; ate very little.

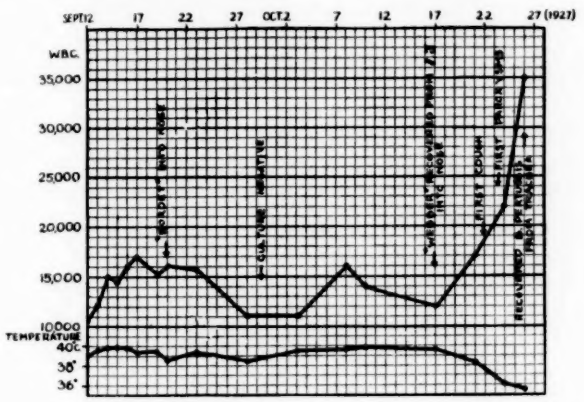

Chart 7 (monkey 8).—No symptoms or blood changes following inoculation with old strains of B. pertussis. Symptoms and marked leukocytosis followed the inoculation of B. pertussis recovered from monkey 7. Cultures from the tracheal wall were positive for B. pertussis.

October 12: Coughed nine times within a few hours, usually four to six hacks in a paroxysm; appeared very ill.

October 14: Killed by the injection of air into the heart; at autopsy, hemorrhage or lesion was not found in the larynx or trachea. Several small areas of consolidation were found in the lower parts of both lungs; *B. pertussis* was isolated from these consolidated areas. *B. pertussis* thus recovered was inoculated into monkey 8.

Monkey 8.—*Macacus rhesus* monkey, male, arrived on Sept. 3, 1927; weight, 1,320 Gm.; hemoglobin, 70 per cent.

September 9 to 19: Average leukocyte count, 14,050; polymorphonuclears, 48; lymphocytes, 50; eosinphils, 2.

September 20: Strain "Bordet" dropped into nares (chart 7).

September 23: Strain "Bordet" dropped into nares.

September 30: Deep throat culture negative; average leukocyte count for previous sixteen days, 13,891; cough did not follow.

October 17: Cough not present; *B. pertussis,* recovered from monkey 7, was dropped into nares.

October 22: First cough; eight paroxysms; enteritis.

October 24: First severe paroxysms; from six to eight hacks in paroxysm; appeared ill; enteritis more severe.

October 25: Cough more frequent and severe; from six to eight hacks in close succession; enteritis continued.

October 26: Bent forward when coughing; rhinitis and enteritis persisted; killed. At autopsy, the larynx and trachea appeared normal; the lungs appeared normal except for a hemorrhagic, consolidated area in lower lobe of the right lung, 2 by 1.5 cm.; colon inflamed; two ulcers measure 2 by 1.5 cm. Cultures from the tracheal wall were positive; cultures from the normal lung, the consolidated area of lung and blood from the heart were negative.

CONCLUSION

After a period of incubation of from one to three weeks, spontaneous, paroxysmal coughs followed the injection of *B. pertussis* (Bordet-Gengou) into the larynx of five healthy young monkeys. Similar coughs followed inoculation into the nares of three healthy young monkeys. The white cell and differential blood counts usually showed the transient lymphocytosis characteristic of pertussis in human beings. The bacillus was recovered from deep throat cultures; also from the larynx, trachea and lungs after death. The bacillus was recovered during the height of the cough from an animal that had been inoculated with the bacillus recovered, in turn, from the lung of another coughing animal. Animals which recovered were immune to subsequent injections of various strains of *B. pertussis.*

ATROPINE FEVER IN EARLY INFANCY*

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ST. LOUIS

My object in this paper is to emphasize by discussion a fact which is already known, but which has acquired new importance with the increasing use of atropine in the so-called "true colic" of early infancy; namely, that in certain cases, atropine produces an abrupt rise in temperature, even in average dosage.

INDICATIONS FOR THE USE OF ATROPINE IN EARLY INFANCY

Before considering the frequency and the mechanism of this pyrexia, one should review for a moment the conditions for which atropine is commonly given to infants. There are principally two: pyloric stenosis and gastro-enterospasm, commonly miscalled pylorospasm.[1] In a previous paper,[2] the statement was made that atropine will cure the majority of patients with functional vagogenic gastro-enterospasm. The principal manifestations of this condition are (*a*) extreme fretfulness, aggravated by feeding, with inability to nurse because of cramps or "colic," with (*b*) occasional projectile vomiting, plus diarrhea or constipation, with or without visible gastric or intestinal peristalsis and (*c*) without the olive-shaped tumor of organic pyloric stenosis. It is to infants with any or several of these manifestations that atropine is most commonly and most successfully given.

The average gastrospastic or enterospastic infant under 3 months of age can readily tolerate from 1 to 2 minims of a fresh 1:1,000 solution (0.065 to 0.12 mg.) of atropine sulphate given in a little water twenty minutes before each feeding. The administration of this drug, however, requires many warnings to parents as to the variability of reaction. Some infants need enough to produce a flush. Some will

* Submitted for publication, Oct. 9, 1928.

* Read before the St. Louis Medical Society, Sept. 25, 1928.

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1. Preoperatively, in combination with morphine, atropine is apparently not given to children as often as to adults. I suspect, however, that at least a few patients with "postoperative febrile reactions" are really suffering from atropine fever. Pulmonary edema, another infrequent indication for the use of atropine in infancy, is so severe a condition, if not "terminal," that a reaction due to the drug itself would be difficult to trace. In asthma, atropine fever could probably be detected. Asthma, however, is so rare during the first few months of life that no cases for study were encountered.

2. White, P. J.: Gastro-Enterospasm as a Manifestation of Autonomic Imbalance in Early Infancy, Am. J. Dis. Child. **26**:91 (July) 1923.

flush after the first dose, others after later doses. The time and extent of pupillary dilatation vary with the infant. Even the degree of the much desired gastro-intestinal relaxation will vary; whether a given patient will have fever with these manifestations is impossible to predict.

INCIDENCE OF ATROPINE FEVER

In order to determine, if possible, the incidence of fever in young infants receiving atropine in the dosage mentioned, I have examined a number of hospital records and a number of records from private practice. Let me emphasize that patients of this type are seen much more commonly in private and dispensary practice than in the wards. Unless they develop secondary infections or unless they have true pyloric stenosis and are therefore refractory to atropine, they are not likely to require treatment in the hospital.

Four, or 13.8 per cent, of twenty-nine patients in the hospital with bona fide gastro-enterospasm, without parenteral infection, developed fever unquestionably due to the use of atropine. Three, or 9.4 per cent, of thirty-two private patients developed fever due to atropine. None of the twenty-two patients in the hospital with uncomplicated congenital pyloric stenosis, all given atropine, developed fever. A number of these were on thick cereal feeding. The hospital figures are necessarily low because of the exclusion of patients presenting secondary infection, athrepsia, anhydremia and similar disturbances.

It is interesting that two of the patients in the hospital with uncomplicated gastro-enterospasm developed leukocytosis after the administration of atropine; one had 17,800 white cells and the other 12,000. Benzing [3] reported that leukocytosis may follow the administration of atropine.

REPORT OF CASES

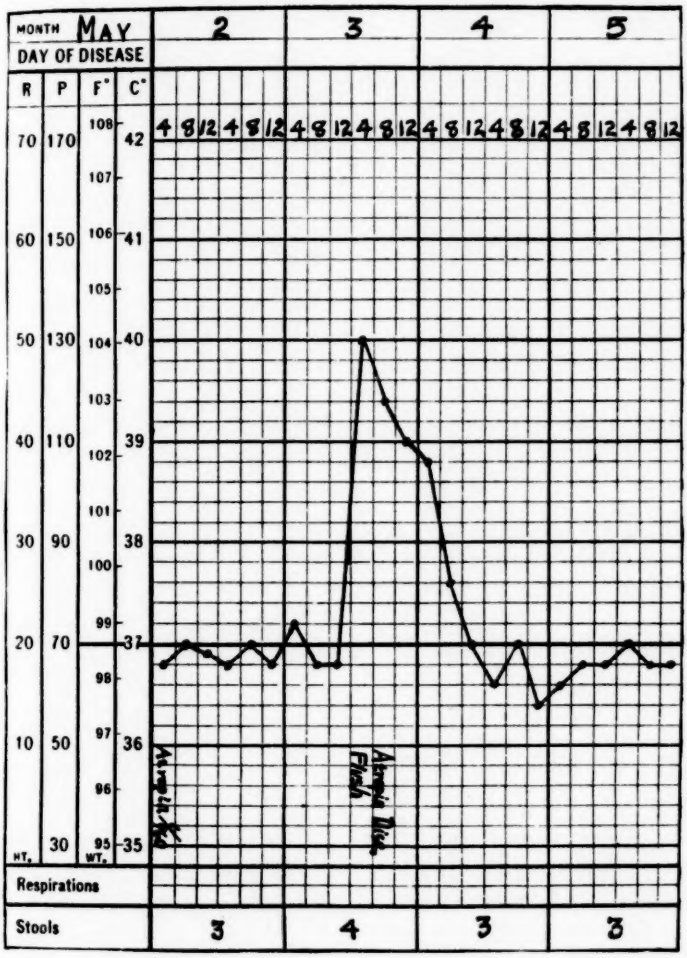
To give minute details, or to multiply case reports, would be tedious and unprofitable; therefore, I shall present only two cases in outline.

CASE 1.—Carroll M., a boy, aged 5 weeks, was seen on July 4, 1928, in consultation. He had been breast fed for two weeks, and then given lactic acid milk and corn syrup. During the week prior to admission, he was given lactic milk, barley water and syrup; he had seven or eight loose stools a day; he "strangled," vomited a large amount of each feeding, and screamed with pain after each feeding. The vomiting grew steadily worse. The administration of atropine was started five days prior to admission. On admission, the temperature was 99.6 F. (37.6 C.). The leukocyte count was 18,200. The pupils were equal, and reacted well to light. There was no flush. The temperature promptly rose to 102.2 F. (39 C.). There

3. Benzing, R.: Ueber Atropinfieber bei Säuglingen, Monatschr. f. Kinderh. **24**:509 (Jan.-Feb.) 1923. Backman, E. L.; Edstrom, G.; Grabs, E., and Hultgen, G.: Compt. rend. Soc. de biol. **93**:190 (June 26) 1925; abstr., J. A. M. A. **85**:856 (Sept. 12) 1925.

was no evidence of infection. The use of atropine was discontinued immediately. The next day the maximum temperature was 101 F. (38.4 C.), after which it remained normal. The infant was given thick cereal feeding and made a rapid recovery.

CASE 2.—Josephine B. began projectile vomiting when 3 days old. There was evidence of neither intracranial hemorrhage nor infection of any kind. She was



Febrile reaction in case 2 after the administration of a dose of 1 minim of 1:1,000 solution of atropine.

breast fed, with complementary feeding of lactic acid milk and corn syrup. Her febrile reaction to the dose of 1 minim of 1:1,000 solution of atropine (0.065 mg.) did not occur until thirty-two hours after the administration of atropine was begun—as shown in the accompanying chart. At that time she was flushed and her pupils were well dilated. The use of atropine was discontinued shortly after the fever reached its height. For some unknown reason, the vomiting did not recur. Thick cereal feeding was not necessary.

COMMENT

It would require no great amount of courage to continue atropine therapy in the face of a febrile reaction in order to determine whether the establishment of tolerance would not result in a fall in temperature. I am confident this would be the case. It is hard to conceive that the abrupt fever in these patients is due to anything but stimulation of the temperature regulating centers in the brain—a degree of stimulation out of proportion to the dose. The dose given the first patient was not sufficient to paralyze the pupillary contraction, nor was it sufficient to produce a flush. Yet the temperature rose abruptly to 39 C. (102.2 F.).

Although every pediatrician and pharmacologist with whom I have talked about atropine fever seems familiar with the phenomenon, the only article devoted to the subject which I can find in the literature is the excellent one by Benzing [3] aforementioned.

According to this observer, infants tolerate atropine better than do adults. Those who are sensitive to atropine react to ordinary doses, with a rise of temperature to 38 or 39 C. (100.4 or 102.2 F.) Diminished tolerance may be present when the feeding is concentrated, with a resultant low water content. (This was not observed in any of my patients.) Benzing considered that infants somewhat dried out from vomiting are especially likely to react with fever, and that tolerance may be increased by the gradual increase in dosage.

It has been my experience that concentrated thick cereal feeding need be started only in those cases in which atropine has failed or has produced a severe reaction. It succeeds so regularly in such cases that it might seem best to resort to it before using atropine instead of afterward. There could be no objection to this procedure with artificially fed infants. But when breast milk is obtainable it seems wiser to use it as food, avoiding if possible the difficult task of pumping the breasts and boiling the milk down with farina.

The length of time required for the production of fever with atropine seems to vary. According to Benzing, the fever usually starts three or four hours after oral or subcutaneous administration—with the peak in from six to eight hours—and disappears after the drug is discontinued. In the first of the two cases I have presented, several days were required; in the second, thirty-two hours.

MECHANISM OF ATROPINE FEVER

Though so marked and so abrupt a rise of temperature as that in atropine fever would seem to be due to a central action, independent of the well known suppression of sweating, the whole question of the function and even of the existence of a temperature center is still a

matter of debate. Howell [4] doubted the existence of any one center, considering that there are several coordinating systems involved. He cited Zuntz's case of a man without sweat glands who developed high fever on making the slightest effort in warm weather. Such a condition is analogous to that of the struggling, effort-making infant, deprived by atropine of his ability to perspire. By this analogy, however, all such infants should develop atropine fever. Certainly, less than 10 per cent of them do so.

Sollmann [5] admitted that the "constancy of the temperature of the warm-blooded animals is obtained through nervous mechanisms, certain portions of the mid-brain, the corpora striata and the caudal nuclei being especially important, so that they have been designated as 'temperature centers.'" He maintained, however, that "atropin hyperthermia may fairly be attributed to the muscular excitement, and to the suppression of sweat."

Solis-Cohen and Githens [6] stated emphatically that atropine fever is "not secondary to circulatory changes or tremors, but has been shown experimentally to result from increased heat production due to direct stimulation of the heat-producing center (Meuriot)." Similarly, Cushny [7] (quoting Ott) said that the dissipation of heat is increased, but that heat formation undergoes a still greater augmentation. This is attributed to direct action on the heat centers of the brain.

From these observations, it does not seem illogical to suggest that the effect of atropine be tried experimentally in patients with lesions in the region of the so-called basal ganglia where the temperature-regulating centers are supposed to be—for example, in patients with congenital athetosis. Patients with certain types of lesions of the brain are known to have labile temperatures. It would be most interesting to learn whether atropine can regularly produce fever in such patients.

Finally, though one is accustomed to associate fever with flushing, one must bear in mind that such increased cutaneous circulation is really an attempt at reduction in temperature. According to Lindberg,[8]

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4. Howell, W. H.: Text-Book of Physiology, ed. 7, Philadelphia, W. B. Saunders Company, 1913, p. 938.

5. Sollmann, T.: Manual of Pharmacology, ed. 3, Philadelphia, W. B. Saunders Company, 1927, p. 574.

6. Solis-Cohen, S., and Githens, T. S.: Pharmacotherapeutics, New York, D. Appleton & Company, 1928.

7. Cushny, A. R.: Text-Book of Pharmacology and Therapeutics, Philadelphia, Lea & Febiger, 1924. Heffter: Handbuch der Experimentellen Pharmacologie, Berlin, Julius Springer, 1924, p. 640.

8. Lindberg, G.: Action of Atropin in Infants, Acta Paediat. **4**:309 (July 1) 1925; abstr., J. A. M. A. **85**:938 (Sept. 19) 1925.

the strong vasomotor reaction of atropine is constant in the healthy person, and seems to be a compensating phenomenon to counteract the temperature-raising action of the drug.

CONCLUSIONS

1. The vasomotor effect of atropine may produce apparent fever.

2. The less common central effect of atropine may produce real fever, which occurs within a variable length of time after the administration of the drug has been started, but which disappears promptly when the drug is discontinued.

3. In spite of the occasionally striking by-effects of atropine, it remains a safe drug for use in the vagogenic gastro-enterospasm or "colic" of early infancy.

PREMATURE INFANTS

A CLINICAL AND PATHOLOGIC STUDY *

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In a recent review of the literature I found few attempts to correlate the clinical and pathologic changes observed in premature infants. In the period covered by this study, 102 infants were under observation in the Premature Station of the Sarah Morris Hospital. The care and feeding of this same group of premature infants was discussed by Hess and Chamberlain. Fifty-four infants of this group were discharged from the station in good condition; forty-eight died, and a complete necropsy was performed on thirty-six. In these, the pathologic processes found were studied with the clinical course as a background in an effort to evaluate the symptoms which had been in evidence. The histories and observations of the infants who died were reviewed from the clinical and pathologic point of view in an attempt to use the information thus gained in furthering the survey of the group that lived, more particularly with reference to the symptoms manifested by the latter during their stay in the hospital and the subsequent period, during which time they were under observation.

Complete physical examinations were made of all infants as soon after admission as their condition warranted. Certain features noted in the course of clinical observation, especially in the early cases under observation, have been of great assistance in drawing conclusions as to diagnosis, and more especially prognosis.

MAJOR CLINICAL SYMPTOMS

Cyanosis.—In the tabulation of the clinical symptoms, cyanosis occurred with such frequency that a special study was made of this symptom. In the series of 102 infants, marked cyanosis was observed in fifty-three or 51 per cent of the total. Forty-six of the infants died. Only two of the infants who died did not exhibit cyanosis at some time during the course of the illness. In the infants who lived, cyanosis occurred as a single attack or as an occasional attack associated with some demonstrable cause such as hypothermia, hyperthermia, vomiting during feedings, and, in the presence of abdominal distention, exhaus-

* Submitted for publication, Oct. 16, 1928.

* At the Premature Station, Sarah Morris Hospital for Children of the Michael Reese Hospital, and the Nelson Morris Institute for Medical Research, Chicago. This study was made possible by a fund from the Infant Aid of Chicago.

tion, diarrhea and infections. Severe forms were recorded seven times in the group of patients who lived. In one of these, the infant had intermittent cyanotic attacks during the first few days with marked apathy and difficulty in feeding. Later, this infant had an uneventful convalescence and at the age of 17 months was apparently normal, physically and mentally. The condition was diagnosed as intracranial hemorrhage, but it was never proved that the diagnosis was correct. Temporary attacks of a minor degree are not an uncommon sign in the premature infant who lives.

Cyanosis was the most outstanding symptom in the patients who died. Careful record was made of the time of occurrence, length of attack; frequency and as to whether the cyanosis was precipitated by any definite cause. It was soon evident that most cases in which cyanosis occurred could be definitely grouped, with regard to type, time and

TABLE 1.—*Classification of Cyanosis*

Type of Cyanosis	No. of Cases	Average Death, Days	Age of Admission, Days	Average Admission Temperature	Average Months Premature	Average Birth Weight, Gm.	Pathologic or Clinical Diagnosis
I. Continuous.....	6	1.5	New-born	96.2	0.75	1,780	Atelectasis
II. Intermittent attacks							
(a) From 1-3 days	19	2.77	1	94.4	6.8	1,306	Infratentorial hemorrhage
(b) 1-3 and again from 7-18 days	6	19.3	Above one week	98.0	7.0	1,657	Hemorrhage plus infection
III. Terminal.....	13	31.0	Above one week	....	7.25	1,776	Infection

frequency of occurrence as a basis. This led to an attempt to establish a classification of this symptom based on a correlation of the clinical and pathologic observations.

(1) Continuous Cyanosis: This type of cyanosis was continuous and progressive from the time of birth to the time of death, and involved the whole body. It occurred in six cases, in four of which necropsy was performed. Of the latter, three showed marked atelectasis and the fourth marked atelectasis in addition to severe intracranial hemorrhage. The average age at death was 1½ days. The remaining two cases in this series were diagnosed clinically as atelectasis. One case was an exception in that it showed marked atelectasis at autopsy, although this infant had had frequent severe attacks of cyanosis rather than the continuous type.

(2) Intermittent Cyanosis: In all of these cases cyanosis occurred in severe attacks, sudden in onset, with marked prostration, and lasted from a few seconds to ten or fifteen minutes. Between attacks, the skin frequently had a marked purplish-red tinge; this was noticeable especially in those infants who died during the first two days. Two types grouped according to the age at death were noted.

(*a*) Those who Died in the First Three Days: Nineteen infants had repeated attacks varying in number from two to fifteen in twenty-four hours, all occurring prior to the third day, by which time death occurred. Fourteen necropsies were performed in this group, a definite subarachnoid hemorrhage below the tentorium, especially marked about the cerebellum or brain stem or both, was found in each case. Seven infants in this group also had some cortical hemorrhage. The remaining four did not come to necropsy, but the condition was diagnosed clinically as intracranial hemorrhage. Of this entire group exhibiting the same type of cyanosis, it was interesting to note that only one infant who came to necropsy did not show intracranial hemorrhage.

In another series of cases studied at a later period, in which the intermittent cyanotic attacks were similar to those described in group A, the days of life were seemingly prolonged by early and repeated spinal drainage. A needle of small caliber was used.

(*b*) Those Who Died After the Tenth and Before the Twenty-Seventh Day of Life: This group had cyanotic attacks occurring from the first to the third day, similar to those in group A, although usually not so severe. Then followed a free interval in which attacks did not occur until about the seventh day. From the seventh to the eighteenth day, which was the usual length of life, there was a recurrence of the attacks, which became more frequent prior to death. In all probability, infection was a contributing factor. There were six cases of this type, in five of which a pathologic examination was made; infratentorial hemorrhage as described in the foregoing observations was noted in all the cases, in addition to an overwhelming infection and sepsis, such as purulent otitis media, mastoiditis and pneumonia. One case which was not examined post mortem was diagnosed clinically as otitis media and probable intracranial hemorrhage. Several infants in this group were severely jaundiced before death. Apparently they temporarily resisted the effects of the hemorrhage, then, owing to their lowered resistance, developed an infection which proved fatal.

(3) Terminal Cyanosis: This type of cyanosis occurred usually within a few hours to a day or two days of death, in more or less mild to severe form, becoming more severe just before death as the child became weaker. In practically every instance some definite cause could be found to account for the cyanosis, such as infection and accompanying complications as distention, exhaustion, vomiting and severe diarrhea. When cases of this group came to necropsy they showed evidence of severe infection, such as purulent otitis media and mastoiditis, pneumonia, tuberculosis and syphilis. In three cases in which a necropsy was not performed, the clinical diagnosis was pneumonia.

(4) Sporadic or Occasional Cyanosis: In one infant with a congenital heart anomaly, which was confirmed by autopsy, an occasional

attack of cyanosis occurred at varying intervals, from the time of admission on the fifth day, to the time of death on the eighteenth day. This was present usually with the feedings or vomiting and was undoubtedly due to the extreme weakness of the infant. Two infants with congenital heart disease, who are living at the present time, did not exhibit cyanosis at any time during observation.

Recently two cases, not included in this series, presented an entirely new picture. An infant boy, M., was cyanotic on admission just after birth. This was thought to be due to a temperature of 95 F. He did fairly well for five days, then had a sudden severe attack of cyanosis lasting fifteen minutes. He became progressively weaker and died the next day. At postmortem examination a large, thick thymus, weighing 12 Gm., was found. The suprarenal glands were also large, each weighing 3 Gm. The patient in another case, similar in its history to this one, had a large, thick, leaflike thymus weighing 16 Gm. In these two infants the cyanosis was possibly due to the pressure of a large thymus. Yllpo reported 600 cases without enlargement of the thymus in the entire series. An occasional infant was found who had short attacks of cyanosis only during the first few days; these were usually associated with feeding or vomiting. Primary pneumonia may also produce sporadic cyanosis.

In the group of infants who exhibited cyanosis at birth and during the first few days, and who later showed progress with recurring cyanosis between the seventh and eighteenth day, infection was the common terminal complication. In six of these cases, infratentorial hemorrhage was found at autopsy. Late or secondary hemorrhage was suspected in some of the cases, but in none of them was this verified at autopsy.

The analysis of table 1 shows that in the most immature group atelectasis and intracranial hemorrhage were the most frequently demonstrable pathologic observations as possible causes of death. The importance of the arrested development of other organs, and the resultant inability to carry on their physiologic functions, in all probability contributed to the high and early mortality.

Diarrhea.—Diarrhea was a frequent symptom, occurring in forty-three of the total series of cases, eighteen of which were fatal. In the latter, diarrhea followed infection, which, in many instances, complicated some primary pathologic process such as intracranial hemorrhage. The average age at death in this group was twenty-four days. Of the infants who lived, twenty-five had diarrhea; the condition in most of them, while calling for immediate consideration, was not serious. In ten, this symptom was present on admission. Fourteen cases developed in infants because of overfeeding or secondary to focal infections following admission. Diarrhea was usually the earliest symptom of infection.

Jaundice.—Marked jaundice was a symptom in twenty-three cases of the total series—in thirteen of the infants who died and in ten of those who lived. There were two types of marked jaundice: jaundice which occurs during the first two weeks of life, and which is most often icterus neonatorum, and extreme jaundice, which becomes increasingly evident after the second week. This type was present in fifteen cases.

Infratentorial hemorrhage was complicated by extreme jaundice in five cases. In all of these there was a complicating infection. There was no conclusive evidence that intracranial hemorrhage was the primary cause of the jaundice in this group. Infection appeared to be the predominating factor in the development of icterus in the fatal cases.

Vomiting.—(This analysis will consider only those cases in which vomiting was severe or persisted over a long period of time.)

The vomiting of forty-two infants was of this type. Seventeen cases (40 per cent of those vomiting) occurred in the series in which the patients died. Of this number, two were infants who probably died from infratentorial hemorrhage. This may have been a coincidence. The remaining fifteen deaths were associated with terminal infections or sepsis. In those who lived, marked vomiting usually accompanied infection. Three cases occurred because of pylorospasm. Vomiting in many of the cases with infection was due to the marked abdominal distention and accompanying gastric irritability.

Distention.—Distention is a common disturbance in premature infants, and is most frequently seen in infants who have severe infections. It is to be given serious consideration at all times, as it becomes of grave importance when it is secondary to infection. In those who died, distention became more marked as the infant became weaker. This is a distressing symptom, as it is so often associated with vomiting, hiccup, belching, flatulence and exhaustion, and is usually not relieved unless the infection subsides.

In the group of infants who lived, the major symptoms of those having infections were diarrhea, vomiting, jaundice and distention. Diarrhea and vomiting were associated in most of the cases. Cyanosis was rarely observed in those who recovered.

MINOR CLINICAL SYMPTOMS

Crying.—The quality of the cry is often of help in obtaining a clinical estimate of the infant's vitality. In older infants with intracranial hemorrhage, the cry is often short, sharp and moaning.

Fontanels.—There was no marked bulging of the fontanels in the entire series of 102 cases. The fontanels were usually flush or depressed, dehydration being a probable factor; they were, therefore, of little assistance in the diagnosis of intracranial hemorrhage.

Convulsions.—Generalized convulsions were noted in four of the infants studied. In three instances, convulsions occurred within a few hours of death as the infections were severe. (Convulsions were probably induced by the exhaustion anoxemia as the patients were relieved immediately by oxygen.) The fourth patient, a child with spasmophilia, recovered. Generalized spasticity, while less frequently seen than would be expected in such a large group of cases, should lead to the suspicion of intracranial hemorrhage.

Twitchings.—These indefinite symptoms occurred at times in infants suffering from various conditions. Numerically, they were not more frequent in the cases in which hemorrhage occurred than in the others. This was probably accounted for by the early death among the patients with severe cases of intracranial hemorrhage.

Apathy.—Marked apathy was present at times in all infants who died, especially those in the group with intracranial hemorrhage. It was present to a lesser degree in all living infants.

Eye Changes.—Definite changes could not be noted in the size, shape or reaction of the pupils. Nystagmus was indefinite, and conclusions could not be drawn.

Temperature.—There were nineteen infants with a temperature of over 100 F.; the highest was 103 F. Ten of the living infants had fever, all being associated with infection. Sixty-five per cent of those having infections showed little, if any, rise in body temperature. The infections were chiefly those of the upper respiratory tract, otitis media, pyelitis and pneumonia. In the series in which the patients died, there were nine with a temperature above 100 F., the highest being 103 F. These constituted 50 per cent of the total infections in this group. A rise in temperature does not necessarily occur as a symptom of infection, as some of the most severe examples had a normal or subnormal temperature. Subnormal temperatures are often indicative of a poor prognosis, especially in the smaller infants.

Difficulty in feedings, regurgitation and irregular respirations were noted frequently in all types of cases.

Other conditions observed in the series in which the patients lived were as follows: pylorospasm, three cases; alimentary intoxication, three; syphilis, three; congenital heart anomaly, two (one associated with syphilis and one with megacephaly, with no cyanosis in either case); rickets, three; spasmophilia, one; hernia, one; miliaria (severe), one; and hematoma above the clavicle, one.

Infections.—Acute infections occurred in fifty cases. Eighteen patients in this group died; in these, the infection was usually a terminal process or a secondary complication of some primary pathologic lesion present at birth.

These primary lesions were: infratentorial hemorrhage, seven; tuberculosis, two; syphilis, one; congenital heart anomaly, one; in seven cases other complications were not present but the patients died from primary otitis media and mastoiditis, pyelonephritis, pneumonia or other infection. In the living series, there were thirty-two cases of infection, the condition in many of them being present on admission. Several had mild infections lasting a few days, and twenty-two had severe infections; many had multiple foci.

Otitis media was the most frequent type of infection, occurring as catarrh in most cases, while others were opened or ruptured spontaneously. Next in order of frequency were rhinopharyngitis, conjunctivitis, cord infections, pyelitis, pneumonia and furunculosis. Enteral infection was usually secondary to these conditions.

Several foci of infection occurred in the same infants, such as otitis, pyelitis and omphalitis or other combinations of these infections. It is significant that the infants who recovered often had multiple foci of infections at the same time. Pneumonia, primary or secondary, usually the latter, was most serious—seven of eight patients dying as a result of this condition.

The infants who lived were usually older and heavier and consequently had greater resistance.

CLINICAL SUMMARY

1. Clinically, cyanosis in premature infants is the most important symptom and is of great diagnostic and prognostic value. The major pathologic processes, such as infratentorial hemorrhage, atelectasis and infections, can often be diagnosed on the basis of the type of cyanosis. A tentative classification of cyanosis is presented as a basis for future study of similar groups of cases:

(*a*) Continuous cyanosis, most often due to atelectasis.

(*b*) Intermittent cyanosis occurring during the first few days, usually the result of infratentorial hemorrhage.

(*c*) Antemortem attacks occur often in infants dying of infection.

(*d*) Sporadic cyanosis for which some other cause can often be definitely discerned at the time of attack.

2. Severe diarrhea occurs more often as a complication secondary to systemic or focal infection than as a primary condition in breast-fed infants.

3. Jaundice may occur in severe form after the first week, usually as a symptom of infection and sepsis, which may be associated with intracranial hemorrhage.

4. Vomiting of severe type is often associated with infection and sepsis.

5. Distention is often a result of these symptoms and is associated with them.

6. There are no other symptoms that are regularly of any definite diagnostic or prognostic value. Signs of increased intracranial pressure as noted in full-term, new-born infants, such as bulging fontanels, convulsions and twitching, are infrequent in premature infants having intracranial hemorrhage, although these symptoms may occur.

7. Elevations of temperature occurred in only about one third of the infants having infections: subnormal temperatures were frequently observed.

8. Infections occur in various forms: otitis media is the most frequent. Pneumonia is the infection which is most fatal.

TABLE 2.—*Relationship of Major Pathologic Lesions to Associated Pathologic Lesions*

Pathology	No. of Cases	Infratentorial Hemorrhage	Supratentorial Hemorrhage	Cardiac: Patent Foramen Ovale	Cardiac: Patent Ductus Arteriosus	Atelectasis (All Degrees)	Acute Infection	Syphilis	Pneumonia	Tuberculosis
1. Infratentorial hemorrhage...	18	..	9	8	6	11	5	0	2	0
2. Supratentorial.....	12	9	..	4	3	7	2	1	1	0
3. Atelectasis.....	18	11	7	7	3	..	4	1	0	0
4. Acute infection.....	15	5	2	2	0	4	..	1	2	1
5. Cardiac										
Patent foramen ovale.....	13	8	4	..	6	7	2	1	1	1
Patent ductus arteriosus...	9	6	3	6	..	3	0	2	1	1
Both.....	6	3								
6. Pneumonia (primary).....	4	2	1	1	1	0	2	1	0	0
7. Syphilis.....	4	0	0	1	2	1	1	..	1	0
8. Tuberculosis.....	2	0	0	1	1	0	1	0	0	

PATHOLOGIC STUDY

We have attempted to show that certain symptoms are dependent on a definite process. In all cases in which necropsy was done, the pathologic lesions were correlated with the symptoms manifested ante mortem. The pathologic processes found at autopsy were classed as major or associated lesions. Many infants exhibiting the same clinical symptoms were found to have the same pathologic lesion at autopsy. Therefore, this lesion was said to be the major pathologic process and the chief cause of death. Other lesions present in the same infant were referred to as associated pathologic processes. They did not produce any regularly characteristic symptoms. The relationship between what is referred to as the chief pathologic process and the associated pathologic processes illustrates the fact that most of the premature infants who died had more than one pathologic lesion.

From table 2 it is seen that of the eighteen patients having infratentorial hemorrhage, nine also had supratentorial hemorrhage, eleven

showed some degree of atelectasis, eight had patent foramen ovale, six had patent ductus arteriosus and five had infections. I was led to believe that infratentorial hemorrhage was the chief cause of death, in view of the fact that every one of these infants had the same symptom, namely, intermittent cyanotic spells, whether or not any of the other associated pathologic processes were present. Many combinations of lesions were present in the same patient, as illustrated in table 2.

Table 3 shows the combination of associated lesions in the patients also having infratentorial hemorrhage, the clinical course in every case being characterized by the one outstanding symptom of intermittent cyanosis. Except in one case of atelectasis which gave a similar clinical picture, this type of intermittent cyanosis was not found in any other series, regardless of the presence of one or more of the other pathologic processes already mentioned, unless hemorrhage occurred below the tentorium. In considering intracranial hemorrhage, the infratentorial type was separated from the cortical type, purely on a symptomatic basis,

TABLE 3.—*Combination of Lesions Associated with Infratentorial Hemorrhage*

All cases having as the most prominent symptom intermittent cyanosis	
I. Infratentorial hemorrhage, atelectasis, patent foramen ovale, patent ductus arteriosus	3 cases
II. Infratentorial hemorrhage, cortical hemorrhage	3 cases
III. Infratentorial hemorrhage, cortical hemorrhage, atelectasis	1 case
IV. Infratentorial hemorrhage, cortical hemorrhage, atelectasis, patent foramen ovale	4 cases
V. Infratentorial hemorrhage, infection (one case with cortical hemorrhage)	4 cases
VI. Infratentorial hemorrhage, atelectasis (moderate)	3 cases

since the latter type did not produce any evident symptoms. Six different combinations of infratentorial hemorrhage with other lesions were noted in the eighteen cases. In three, the hemorrhage was associated with a moderate degree of atelectasis and patent foramen ovale and ductus arteriosus; in three others, there was a hemorrhage over the cerebral cortex and also an infratentorial hemorrhage. In one case infratentorial hemorrhage was associated with atelectasis and cortical hemorrhage; in four, with cortical hemorrhage, atelectasis and patent foramen ovale; in four others, with infection and in three, with moderate atelectasis. From this analysis it seems reasonable to conclude that moderate atelectasis, cortical hemorrhage, patent foramen ovale or ductus arteriosus and terminal infections do not appreciably change the major symptoms when the chief pathologic process present consists of an infratentorial hemorrhage.

The individual lesions will now be considered.

Infratentorial Hemorrhage.—Infratentorial hemorrhage occurred usually over the cerebellum and generally on its anterior surface. In about one third of the cases, the hemorrhage extended to the pons and medulla. It was subarachnoid in all cases, sometimes consisting of just

a thin layer of blood and at other times of a thick clot. It was either fluid or clotted, depending on the age of the hemorrhage, and the color varied from bright red to greenish brown, depending on the degree of chemical change and absorption. Grossly, the meninges were frequently edematous and hemorrhagic. Occasionally, the vessels of the cortex of the brain were congested. Tentorial tears were not noted. In many cases there was a subdural hemorrhage about the spinal cord. The typical microscopic picture of hemorrhage occurring around the cerebellum is as follows: "Underneath the arachnoid and in the pia is considerable blood. Both layers of the membrane are thickened as the result of proliferation of large mononuclear cells many of which contained phagocytic blood pigment. The capillaries of the pia are greatly dilated but there is no hemorrhage immediately under the pia itself. The brain tissue is normal in appearance."

Cortical Hemorrhage.—Cortical hemorrhage was usually located over the parietal regions, occasionally over the occipital lobes, and varied in consistency and coloring depending on the age of the hemorrhage. In no case did the hemorrhage cause symptoms of increased intracranial tension, such as excessive vomiting, convulsions or bulging fontanels. Cortical hemorrhage was noted in twelve infants, in nine of whom there was also infratentorial hemorrhage. The tenth patient also had otitis media; the eleventh, atelectasis, and the last, syphilis. Cortical hemorrhage did not occur alone in any case, but was always associated with some other pathologic processes as noted in table 3. Apparently cyanosis, or other characteristic symptomatology, did not result from this type of hemorrhage. Cortical subarachnoid hemorrhage may have some degenerative effect which is not manifested until the infants are much older, but immediate symptomatic effects are slight, unless the hemorrhage is extensive.

The spinal fluids are invariably golden yellow. At times, when withdrawn shortly after birth, the fluid may be distinctly bloody. This phase was discussed in a paper recently published by Glaser.[1]

Atelectasis.—Atelectasis was present in eighteen cases in a slight to a marked degree, but in only three was the atelectasis so extreme as to be considered the chief cause of death. These infants had continuous progressive cyanosis terminating in death. One patient also had a massive cortical hemorrhage with the same symptoms as in the other cases. In one infant with marked atelectasis, cyanosis occurred as intermittent attacks. Hemorrhage was not found in this case. In the remaining cases in which the atelectasis involved only a minor to a moderate degree of lung tissue, the condition was termed physiologic and depended on

1. Glaser, J.: Cerebrospinal Fluid of Premature Infants, Am. J. Dis. Child. **36**:195 (Aug.) 1928.

the degree of immaturity of the infant. This has been discussed by other authors. In those cases in which atelectasis was probably the chief cause of death, the amount of inactive lung tissues was far greater than in the other cases.

Patent Foramen Ovale and Ductus Arteriosus.—Patent foramen ovale and ductus arteriosus, whether occurring alone or together, did not seem to influence the symptom complexes or the prognosis. Although patent foramen ovale occurred in thirteen cases, patent ductus arteriosus in nine cases and both lesions in six, they did not produce any characteristic symptoms. The diagnosis of patent foramen ovale and patent ductus arteriosus was made only post mortem, as there were no physical observations referable to the heart at any time. Roentgen examination in several cases did not show any cardiac anomaly. Only one example of congenital heart anomaly occurred in the infants who died, and in this case the symptoms plus the physical observations left no doubt as to the clinical diagnosis.

Infections.—Infections were present in fifteen of the cases in which necropsy was performed and occurred with one or more of the other lesions. The infection was considered the probable cause of death only when other definite major pathologic processes, such as infratentorial hemorrhage or atelectasis, were not found. Usually the infections consisted of otitis media, pyelitis, rhinopharyngitis or pneumonia. The cyanosis in this group was characteristic, occurring as one or more attacks within a few days of death. Pneumonia, which was noted in four necropsies, was the chief pathologic process in only one case, being secondary to infratentorial hemorrhage in two cases and to syphilis in the other. In three cases in which the clinical appearances indicated primary pneumonia, necropsy was not performed.

Syphilitic or Tuberculous Involvement.—Syphilitic or tuberculous involvement, when present, was severe and sufficient enough to account for death in view of the immaturity and the extremely low resistance of the infant. In none of the infants with tuberculous or syphilitic infection was there hemorrhage or atelectasis, which is unusual in such immature infants.

Other pathologic changes noted at necropsy included suprarenal hemorrhage (left), two cases; pericardial petechiae, two; pleural petechiae, one; scalp hemorrhage, one; adenoma of the suprarenal gland, two. These lesions may have been incidental and apparently did not have any part in the symptomatology.

The frequency of the lesion which is the chief cause of death is given in table 4. Infratentorial hemorrhage was the most important single pathologic observation and occurred in eighteen cases in which necropsy was performed. As already stated, this was chosen as the chief cause

of death on account of a similar symptomatology in all cases. Otitis media, with or without mastoid infection as confirmed post mortem, was present in six cases, or 16.6 per cent of those that came to necropsy. These infants had had one or more cyanotic attacks within a few days of death. Pneumonia as a primary condition and as the chief cause of death was found in only one case. It was present in six other patients as a terminal infection. In the remaining cases, the chief cause of death was syphilis in four cases (11 per cent); tuberculosis in two (5.5 per cent), and congenital anomalies in two. It is to be noted from this table that 17 per cent of the total number of patients admitted to the hospital who came to necropsy had fatal intracranial hemorrhage. Of the total number, syphilis accounted for only 3.9 per cent; otitis media, 5.88; atelectasis, 2.94, and tuberculosis, 1.9.

TABLE 4.—*Chief Cause of Death in Thirty-Six Cases in Which Necropsy Was Performed*

Chief Cause of Death	Number of Cases	Per Cent of Deaths	Per Cent of Admissions
1. Infratentorial hemorrhage	18	50.00	17.64
2. Otitis media (with or without mastoid)	6	16.66	5.88
3. Atelectasis	3	8.33	2.94
4. Syphilis	4	11.11	3.92
5. Tuberculosis	2	5.50	1.96
6. Pneumonia	1	2.77	0.98
7. Pyonephritis and anomalies	1	2.77	0.98
8. Congenital heart and anomalies	1	2.77	0.98

TABLE 5.—*Chief Cause of Death in Twelve Cases in Which Necropsy Was Not Performed*

1. Infratentorial hemorrhage	6
2. Atelectasis	2
3. Pneumonia	3
4. Otitis media and furunculosis	1

The probable chief causes of death in twelve cases, in which permission for necropsy could not be obtained, are given in table 5. In this group, deductions were based on the clinical course plus laboratory aids. The probable chief causes of death were: infratentorial hemorrhage, six cases; primary infection, four, and atelectasis, two.

All the deaths that occurred in the series are grouped in table 6. In 50 per cent of the patients who died, infratentorial hemorrhage was considered the chief cause of death. The infections, such as otitis media and pneumonia, were present in 22.8 per cent. This figure is somewhat higher than that for the series in which necropsy was performed, but it is to be noted that three of the four patients who died from primary pneumonia are included in the series in which necropsy was not performed. Syphilis was a factor in only four cases, or 8.33 per cent, and tuberculosis in two, or 4.17 per cent. Two cases, one in which

congenital heart and kidney anomaly was present and the other in which multiple anomalies with pyonephritis were noted, are included. Congenital atelectasis was present in five cases, or 10.4 per cent. Compared to the total number of admissions, practically two of every nine infants admitted had infratentorial hemorrhage, as shown at postmortem examination, or by clinical evidence. Otitis media and pneumonia are

TABLE 6.—*Chief Cause of Death in Total of Forty-Eight Cases*

	Number of Cases	Per Cent of Total Deaths	Per Cent of Admissions
1. Infratentorial hemorrhage	24	50.00	23.52
2. Otitis media and mastoids	7	14.50	6.87
3. Atelectasis	5	10.41	4.90
4. Syphilis	4	8.33	3.92
5. Pneumonia	4	8.33	3.92
6. Miscellaneous	2	4.17	1.96
7. Tuberculosis	2	4.17	1.96

TABLE 7.—*Relation of Birth Statistics to Cause of Death*

Chief Cause of Death	Infratentorial Hemorrhage	Otitis Media and Mastoid	Atelectasis	Congenital Heart and Anomalies	Syphilis	Tuberculosis	Pneumonia	Nephritis	Total
Number of cases	18	6	3	1	4	2	1	1	
A. Months									
6 to 7	8	1	2	..	1	..	..	..	12
7 to 8	8	3	1	1	2	1	1	..	17
8 to 9	2	2	..	..	1	1	..	1	7
B. Birth Weight									
Gm. to 1,000	4	..	1	..	1	..	..	..	6
1,000 to 1,500	6	1	1	..	..	..	..	..	8
1,500 to 2,000	5	4	1	..	2	1	..	..	13
2,000 to 2,500	3	1	..	1	1	1	1	1	9
C. Age at Death									
1 day	3	..	2	..	..	..	..	..	5
2 to 7 days	9	..	1	..	1	..	..	..	11
7 to 14 days	2	..	..	..	1	..	..	..	3
14 to 30 days	4	6	..	1	1	1	1	1	15
More than 30 days	..	..	..	..	1	1	..	..	2
D. Temperature on Admission									
90 to 94	2	..	1	..	1	..	..	..	4
94 to 96	6	2	1	..	1	1	..	..	11
96 to 98	6	2	..	1	2	1	1	1	14
98 plus	3	1	..	..	..	1	..	..	5
E. Age on Admission									
New-born	12	2	3	..	3	..	..	..	
2 to 7 days	6	1	..	1	1	..	..	..	
14 to 30 days	..	2	..	..	..	1	1	1	
More than 30 days	..	..	..	..	..	1	..	..	

next most frequent, being present in 10.8 per cent of the total number of patients admitted.

An attempt to correlate the chief cause of death with the immaturity of the infant is made in table 7.

Infratentorial hemorrhage occurred chiefly in infants under 8 months of age, about 50 per cent of this group being less than 7 months. Most of the infants weighed under 1,500 Gm., hemorrhage being relatively more frequent the smaller the infant. Two thirds of the patients,

twelve, were new-born on admission. Twelve infants admitted during the first few days died before they were 7 days old. The temperature on admission was uniformly low, averaging 94 and 97 F.

Two of the three cases of atelectasis occurred in infants under 7 months of age, the other in an infant 7½ months old. The weight varied between 1,000 and 2,000 Gm. All of the infants were new-born on admission; two died on the first day, the third, on the second day. The temperatures on admission were low, being between 94 and 96 F.

Syphilis was present in four cases, usually in the heavier infants, those weighing between 1,500 to 2,500 Gm. Three of the four were new-born when admitted to the department. All of these patients died within one month.

Tuberculosis was present in two cases; both infants were premature and were older and heavier than any of those already mentioned. On admission one infant was 26, the other 90 days old. They were brought in because they were not gaining, and died within a few days of admission.

Most of the infections occurred in infants of a fetal age of 7 months and up, and especially in the larger infants who had survived the first two weeks. In this group, the age on admission varied from 1 to 28 days, but the ages of all at death were between 14 and 30 days. Infants surviving the first month had a much better chance to live than the others. Of twenty-seven infants admitted when new-born who died later, twenty were examined post mortem. The following causes of death were found to be present: infratentorial hemorrhage, twelve; atelectasis, three; syphilis, three; otitis media and mastoid infections, two. This illustrates the fact that eighteen of twenty patients died of causes over which no control could be exerted, namely, intra-uterine or birth lesions; the remaining two died of acquired infections. In nine infants admitted between the ages of from 2 to 7 days, the following were the causes of death: infratentorial hemorrhage, six; atelectasis, one; syphilis, one; infection, one. Two of the infants, between the ages of 7 and 14 days, died of infections; four from 14 to 30 days old on admission died from varied causes, such as otitis media, nephritis, syphilis and tuberculosis; one infant did at the age of 90 days from tuberculosis.

One half of the total number of patients died before they were 7 days old from causes directly due to immaturity and injury at birth or both. Between the first and second week, there were the fewest number of deaths; after the second week, infections accounted for most of the deaths.

PATHOLOGIC SUMMARY

1. Certain pathologic lesions produce a constant symptom-complex in the infant. Other pathologic lesions in the same infant apparently do not cause regular symptoms. The former lesions may be referred

to as the chief cause of death, because of the fact that they consistently cause the same definite symptom. Infratentorial hemorrhage invariably causes intermittent cyanotic attacks.

2. Infratentorial hemorrhage occurred in 50 per cent of the cases in which necropsy was performed; otitis media, in 16.6; atelectasis, in 8.3; syphilis, in 11.11, and tuberculosis, in 5.5.

3. Pathologic lesions other than the chief lesion usually do not produce any characteristic clinical symptomatology. These lesions include cortical hemorrhage, moderate degrees of atelectasis, patent foramen ovale and ductus arteriosus and mild infection.

4. Atelectasis and infratentorial hemorrhage affect chiefly the most immature infants. Both conditions usually cause death within the first three days.

5. Acquired infections occur in older and heavier infants usually after the first two weeks. The infants with tuberculosis and syphilis were older and heavier and died at a later age than the infants in the other groups.

6. The infants admitted when new-born or when 1 or 2 days of age that died shortly thereafter showed definite signs of immaturity of the tissues and organs. The usual cause of death was intracranial hemorrhage or atelectasis.

7. The infants admitted after the first week were heavier and older. The more immature infants had already died. These older infants were sent to the hospital because they were not doing well, chiefly on account of poor feeding formulas or infection.

HEREDITARY ECTODERMAL DYSPLASIA (CONGENITAL ECTODERMAL DEFECT)

A REPORT OF TWO CASES *

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I wish to report two cases of patients who present unusual types of multiple congenital anomalies, the tissues affected in both cases having developed principally from embryonic ectoderm. Descriptions of similar patients are not lacking in the dental and medical literature, but the condition has not been specifically called to the attention of pediatricians. In the patients whose cases are to be reported in this paper the paucity of scalp hair, eyebrows and eyelashes, the prominence of the brow and the defects in the development of the teeth were so strikingly similar that one would not hesitate in supposing the cause of the anomalies, however obscure, to be the same in both children. And yet, in race and in several most important clinical respects they differed markedly. These will be discussed in detail.

REPORT OF CASES

CASE 1.—*History.*—H. C., a Jewish boy, aged 14, had been seen from time to time in the outpatient department of the Harriet Lane Home since he was 9 weeks old. The examination recorded was made on May 19, 1928. The patient was the eldest of three children, all boys. His youngest brother, who died from appendicitis in November, 1927, at the age of 2½ years, presented anomalies identical with his own. This brother had defective hair and teeth, and he had never perspired. A roentgenogram of the jaws made at the age of 2 years established the same dental deficiencies shown by my patient. The remaining brother, now 9 years of age, was entirely normal. The patient's father and mother were normal members of large families in none of the members of which anomalies had been observed. At birth the hair of the scalp was exceedingly scant and downy, being described by the mother as "like a feather puff." There was an eruption all over the body; this was followed by desquamation, which was especially marked on the hands, feet and face. Dry snuffles developed at the age of 4 weeks. At 6 weeks of age, he suffered from an acute hyperpyrexia accompanied by convulsions. His mother attributed his recovery entirely to the control of fever with cold sponge baths.

The patient was examined in the hospital at the age of 9 weeks. General scantiness of the hair without any evidence of patchy alopecia was noted. There was marked alopecia of the eyebrows. The skin of the face presented lesions, which were described as a slight papular eruption and made the skin appear thickened. Dry snuffles and hoarseness were observed. A presumptive diagnosis

* Submitted for publication, Nov. 5, 1928.

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of congenital syphilis was made, but was not confirmed by the result of the Wassermann test either at the time or when repeated at the ages of 6 months and 5 years. Antisyphilitic treatment was not given.

Since infancy there had been little change in the amount or character of the hair, and it had remained dry and fine in texture and scant. The patient had never perspired, and suffered much from the heat in warm weather. He frequently had fever after exposure to the summer sun. During the last few years he had formed the habit of carrying a wet handkerchief about with him on hot days with which he mopped his face and head from time to time. Physically, he was a strong and active boy. He had frequently run in short races for his school, but said he was short-winded and could not run long distances.

The eruption of teeth had been exceedingly slow, faulty and incomplete. At the age of 1 year only one upper incisor was in process of eruption. When he

Fig. 1 (case 1).—The character of the hair of the scalp, distribution of the hair of the eyebrows, form and location of the teeth in the front of the mouth and prominence of the supra-orbital ridges are shown.

was 2 years of age, the corresponding incisor on the other side had appeared. By the age of 6 years, the six teeth present in the front of the mouth at the time of examination had made their appearance. At the age of 11, a lower rear molar on the right side erupted. One other mandibular tooth appeared and was subsequently lost, but the location and the age at which this occurred had been forgotten.

The patient's voice had always been hoarse. During early childhood he suffered from many "colds" and infections of the throat. Tonsils and adenoids were removed about five years before the present examination. The senses of smell and taste had always been considered normal.

Mentally, he had always been normal, and his progress in school had been uninterrupted.

Physical Examination.—Examination disclosed a bright Jewish boy 14 years of age whose measurements were as follows: height, 161 cm.; weight, 47.3 Kg.; circumference of the head, 51 cm.; circumference of the chest, 76 cm.; circumference of the abdomen, 67 cm. The temperature was 96.9 F. His appearance was characterized by the thinness of the growth of hair, by flatness of the bridge of the nose and by prominent, thick, protrusive lips. The hypotrichosis together with a finely wrinkled appearance of the skin of the face and incomplete development of the lower half of the face due to dental aplasia tended to make him appear much older than he really was. The body showed a general paucity of subcutaneous fat, but the muscles were well developed.

The skin was everywhere rather dark, especially on the face, which had been exposed to the sun. On the body and extremities it was of fine texture, smooth, glossy and dry. Lanugo hair was not present in these areas. There was no hair on the backs of the hands, and no evidence of hair follicles over the dorsal surfaces of the forearms. A scant growth of normally pigmented pubic hair was noted, but the axillary hair was still absent. Over the calvarium the hair was so scant that the scalp, smooth and shining, was everywhere visible. The hair was light and exceedingly fine and soft. The length of the longest hairs was from 8 to 10 cm., although on top of the head the hair had not been cut for at least two years. It was usually extremely dry, but when examined had been softened by the application of oil. There was a slight growth of fine downy hair on the sides of the face and on the upper lip.

On the face there were many small, slightly elevated, papular lesions which were a little lighter in color than the surrounding skin. The largest measured from 1 to 2 mm. in diameter; the smallest was barely perceptible. None of these lesions were noted on the forehead; they were more numerous about the corners of the eyes, nose and mouth, and a number were scattered discretely over the nose. On the cheeks, lateral to the nasolabial folds, the lesions were extremely numerous and confluent, producing an elevated linear ridge.

The head was of normal size, but the bony prominences were strongly developed. The portion of the calvarium formed by the frontal bones seemed to bulge forward, so that it was palpably raised from the level of the parietal bones along the line of the coronal suture. A similar bulging of the occipital bone produced an elevated surface posterior to the lambdoidal suture. The supra-orbital ridges were prominent, and stood out from the rest of the forehead. The lower portion of the face appeared narrow and small in contrast with the upper.

The ears were small and stood out obliquely from the head. Hearing and vision were normal. The eyebrows were scant, and consisted only of bilaterally represented tufts of fine hair on the medial side of each ridge. The eyelashes consisted of the same fine hair. The bridge of the nose was flat, and its contour broken by an irregular elevation in the middle portion, making it appear as if it had been broken. The nares were large and patent. The mucous membrane was atrophic and surmounted in various places with dry, greenish crusts. There was marked atrophy of the inferior turbinates; the middle turbinates were normal. The septum was not deficient in any respect and a foul smell was not noted. The lips were thick, everted and protrusive, and their vermilion border was well defined.

The alveolar processes of both the maxilla and the mandible were poorly developed. There were only seven teeth—four in the maxilla and three in the mandible. The four in the maxilla were pointed, tusklike projections in the front of the mouth. They were spaced widely apart, inclined sharply forward, and occupied the region normally taken by both incisors and canines. There were no incisors

in the mandible, but both canines were present. In addition, there was a rear molar of normal form on the right side.

The mucous membranes of the mouth and pharynx appeared thin and smooth. The tonsils had been removed. The voice was slightly hoarse. The isthmus of the thyroid was distinctly palpable. The chest was well formed. Both nipples were present. Examination of the heart, lungs and abdomen did not reveal any abnormalities. The genital organs were of normal male form; the phallus was somewhat hyperplastic. The extremities, including the nails, were normal. Neurologic examination did not reveal any abnormalities.

Fig. 2 (case 1).—Lanugo-like character of the hair of the scalp is well shown in this picture, although the presence of an oil applied by the patient masks the appearance of extreme dryness. The prominence of the supra-orbital ridges, the fine quality of the hair of the eyebrows and eyelashes, the flatness of the nasal bridge and the thick protrusive lips are also apparent. The papular lesions on the face do not show well in the photograph.

Laboratory Examination.—The Wassermann reaction of the blood was negative on Feb. 26, 1914, June 15, 1915, and on Feb. 12, 1920. The basal metabolic rate was 10 per cent below normal on Dec. 3, 1927.

Roentgen Examination.—Roentgen examination revealed the chest and extremities to be normal on Oct. 27, 1924; the head unusually large with thick bones and small sella on Oct. 27, 1924; one or two secondary teeth in which eruption had not occurred on June 14, 1923; no signs of teeth in which eruption had not occurred on April 2, 1926.

Summary of Important Observations.—The important observations made were: (1) anomalies identical with those of patient, also shown by one brother; (2) generalized defect of hair growth; (3) defective development of teeth; (4) total absence of perspiration and evidences of at least defective subcutaneous glands; (5) smooth, glossy, dry skin; (6) papular lesions on the face; (7) unusual development of bones of skull and small sella; (8) maldevelopment of bridge of nose; (9) thick protrusive lips; (10) defect of mucous membranes of nose, mouth and larynx, and (11) heat intolerance.

CASE 2.—*History.*—A. T., a white girl, aged 7 years, was admitted to the hospital on March 27, 1928. She had been seen on several previous occasions. An older brother and sister of the patient were both normal, and there was no member of the families of either parent with anomalies similar to the patient's. However, scarcity of hair and a tendency to early loss were common on the father's side. The father himself had deficient hair, and one tooth was imperfectly developed. Two of the father's uncles were known to have had a deficient number of teeth. At birth, the hair of the patient's head and eyebrows was completely absent, and the nails were small and concave. The growth of hair was exceedingly slow and sparse, though more rapid during the last year or two than before. Between the ages of 5 and 12 months, nine teeth erupted; none have appeared since.

Physical Examination.—The patient was a slender, active and bright girl of 7 years whose measurements were as follows: height, 117.5 cm.; weight, 20.2 Kg.; circumference on the head, 51 cm.; circumference of the chest, 53.5 cm.; circumference of the abdomen, 52.5 cm. The temperature was 98 F.; blood pressure, 105 systolic and 80 diastolic. Her appearance was characterized by a high protruding forehead, by a paucity of hair on the scalp and eyebrows and by prominent lips.

The skin was normal and did not show papular lesions of the type presented by the first patient. She perspired freely after exertion. The hair of the scalp was sparse, and stood up so that the scalp was everywhere visible. It was light yellow. The individual hairs were of the lanugo type, being fine, dry and crinkly and showing a slight tendency to curl. The longest hairs were from 10 to 15 cm. in length. The hair of the eyebrows was scant and confined chiefly to the medial side. The eyelashes were fine, pale and sparse.

The calvarium appeared large for the size of the face, and the forehead was high and especially prominent. The supra-orbital ridges were unusually well developed.

The ears were large but normally formed. Hearing was normally acute. The eyes appeared deeply set, being overhung by the supra-orbital ridges. Vision seemed normal. The nose was of normal form, but it may be noted that the portion of the bridge between the eyes was deeply concave. There was no evidence of chronic rhinitis. The lips were prominent and thick; the lower lip was everted. The vermilion border was poorly defined.

The jaws were well developed in view of the fact that most of the deciduous teeth were absent and that none of the permanent teeth had erupted. Only nine teeth were present. Five of these were distributed in the upper and four in the lower jaw. Incisor teeth were not present in the mandible. Lateral to the vacant area were two teeth adjacent to each other on each side, a canine and a first molar. In the maxilla, two misshapen incisor teeth were noted; these were spaced widely apart but symmetrically situated. Their general configuration was that of a truncated cone; they did not have a sharp cutting edge and resembled canines more closely than normal incisors. Posterior to these strange incisors there was a single canine on the right, none on the left. These three teeth in the front

of the upper jaw were inclined forward. The first molars were bilaterally represented. Second molars were not present in either the maxilla or the mandible.

The mucous membranes of the mouth and pharynx were normal. The thyroid was not enlarged. No abnormality of the heart, lungs or abdomen was demonstrable. The genital organs were of normal female form.

The extremities were normal except for the nails. These were all present, but at the nail-beds they tended to be flat and concave rather than convex. They belong to the type which have been described as "spoon nails."

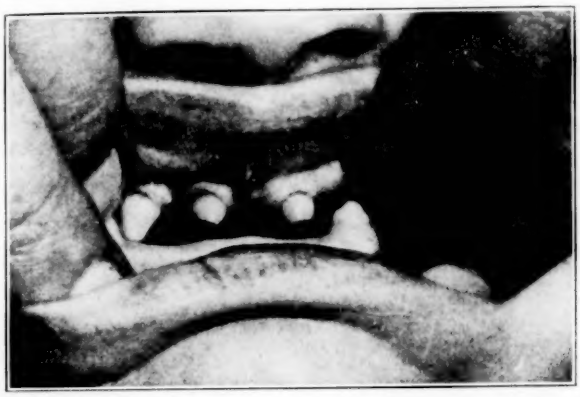

Fig. 3 (case 2).—Character and distribution of malformed teeth in the front of the mouth.

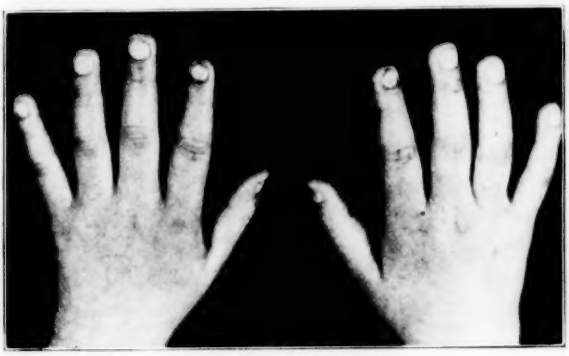

Fig. 4 (case 2).—Character of the nail anomaly.

Neurologic examination did not reveal any abnormal observations. In December, 1926, a mental status determination gave the patient an intelligence quotient of 145.

Laboratory Examinations.—Laboratory examinations revealed: red blood cells, 4,200,000; white blood cells, 7,200 (polymorphonuclear leukocytes, 56 per cent); hemoglobin (Sahli) 65 per cent. The Wassermann reaction of the blood was negative. The urine was normal. The tuberculin test was positive (0.1 mg. injected intradermally). Chemical examination of the blood revealed 10.5 mg. of calcium per hundred cubic centimeters of serum; 5 mg. of inorganic phosphorus

per hundred cubic centimeters of serum; 119 mg. of dextrose per hundred cubic centimeters of whole blood; 560 mg. of sodium chloride per hundred cubic centimeters of whole blood.

Basal Metabolic Tests.—The results of three basal metabolic tests were above normal—59, 37 and 29 per cent, respectively.

Roentgen Examination.—Roentgen examination showed the chest and extremities to be normal; an absence of unerupted teeth in the jaws; a slight degree of convolutional atrophy of the skull and a normal sella.

Summary of Important Observations.—The important observations made in this case were: (1) deficient growth of hair and imperfectly formed or missing teeth in several relatives on the paternal side of family; (2) defective growth of hair, total alopecia at birth; (3) defective development of teeth; (4) congenital anomaly of nails; (5) large calvarium with prominent forehead and supra-orbital ridges; (6) bridge of nose deeply concave; (7) prominent thick lips with vermilion border poorly defined, and (8) elevated basal metabolic rate.

LITERATURE ON CONGENITAL ANOMALIES OF THE TISSUES

Congenital anomalies of all the tissues which arise from embryonic epiblast have been reported. These tissues include the epidermis, the nails, hair, teeth, the glands of the skin, the external organs of sense, as the ear and eye, and the nervous system and the mucous membranes of the mouth, nose and anus. Congenital absence, or congenital defects of some of these tissues, are exceedingly common. Thus, the dental literature abounds with reports of congenitally missing teeth, double rows of teeth, misshapen teeth, etc. The dermatologic literature reveals many cases of congenitally deformed nails and congenital alopecia. In many of these cases an hereditary factor has been noted; in many, the defects have been associated with anomalies of other tissues having a similar ectodermal origin.

One group, to which the first patient belongs, deserves special mention. These are the patients who exhibit congenital absence of the sweat glands in regular association with other ectodermal defects. In 1920, Goeckermann [1] emphasized the fact that these cases form a distinct clinical group. The following is a quotation from his article:

> In one group of cases of high grade congenital ectodermal defect there is not only a congenital absence of the teeth and a hypotrichosis, but also a total absence of sweat glands and an almost total absence of sebaceous glands. This combination gives the cases a stamp which places them in a class by themselves.

In 1924, MacKee and Andrews [2] wrote that they considered the clinical characteristics of the group to be congenital absence of the sweat glands, absence of pilosebaceous apparatus over most of the body,

1. Goeckermann, W. H.: Congenital Ectodermal Defect, with Report of a Case, Arch. Dermat. & Syph. **1**:396 (April) 1920.

2. MacKee, G. M., and Andrews, G. C.: Congenital Ectodermal Defect, Arch. Dermat. & Syph. **10**:673 (Dec.) 1924.

marked dental aplasia, depressed nasal bridge, atrophic rhinitis, prominent supra-orbital ridges, thick protrusive lips, thin, glossy, smooth, dry skin, papular lesions on the face and heat intolerance.

To date there have been only ten examples of patients representing this unusual combination of anomalies described in the literature. (This number does not include members of families said to have been similarly or identically affected but not completely described.) The first of these was reported in 1848, by Thurnam [3] in England. In the words of the author this man, "aged 58, was distinguished throughout life by the almost complete absence of hair, by the teeth being not more than four in number, by the delicate structure of the skin and by the absence of sensible perspiration and tears." Thurnam's detailed account of the physical appearance of his patient and of his discomfort in hot weather is excellent and complete. The results of a postmortem examination are included, this being the only autopsy recorded in the literature although a number of biopsies have been done. In conclusion he said that he "regrets that no observations had been made on the character and amount of the insensible perspiration." Such observations were later to be made on similar patients, and resulted in valuable additions to the knowledge of the mechanism of water loss through the skin.

In the discussion following the presentation of this paper, a second case was described by Williams. Although the description of this second patient was brief, it is sufficient to identify the condition. Because of the importance of the fact that the affected person was of the female sex, I shall quote the essential parts of the description.

> She was fifteen years of age, her hair was fine, scanty and white, and she had scarcely any hair on her eyebrows or any lashes. She had three or four projections resembling teeth, which were decayed. The nose was imperfectly developed, and she breathed with difficulty through the nostrils. She suffered from chronic ulceration of the lining membrane of the nares, attended by a discharge having an unpleasant odor. She had never perspired.

The next patient to be described was reported in 1883 by Guilford,[4] an American dentist. Guilford's report was translated in a German medical journal and in the transcription the name changed to Quilford.[5] This translation has been responsible for some confusion in numbering the reported cases, this patient being listed twice in the tables of MacKee and Andrews. In 1898, Ascher [6] reported two more cases in

3. Thurnam, J.: Two Cases in Which the Skin, Hair and Teeth were Very Imperfectly Developed, Proc. Roy. M. & Chir. Soc. **31**:71, 1848.

4. Guilford, S. H.: A Dental Anomaly, Dental Cosmos **25**:113, 1883.

5. Quilford, S. H.: Eine Zahnanomalie, Wien. med. Wchnschr. **33**:1116, 1883.

6. Ascher, B.: Geschwister mit Anomalien der Ohren, der Zähne und der Haut, Ztschr. f. Ethnol., Verhandl. d. Gesellch. f. phys. Anth., Ethnologie u. Urgeschichte, Sitzung v., 19 Feb., 1898, pp. 114-121.

brothers. The value of this paper is much enhanced by the inclusion of a discussion by Virchow. In 1902, Tendlau [7] added another case. Then in 1911, Loewy and Wechselmann [8] redescribed the two patients previously reported by Ascher and the patient reported by Tendlau. Their reports, besides copying the essential parts of Ascher's paper, disclosed the important fact that Tendlau's patient was an uncle of the two brothers reported by Ascher. Their investigation was concerned chiefly with the mechanism of the production of insensible perspiration. After this, further cases were added by Christ [9] in 1913, by Strandberg [10] in 1918, by Goeckermann [1] in 1920 and by MacKee and Andrews [2] in 1924. The cases reported here bring the total number to eleven.

NOSOLOGY

In reviewing the literature of this subject, I have been impressed by the fact that a complete satisfactory diagnostic term does not exist under which the various ectodermal defects may be grouped. Many reported cases are scattered under descriptive diagnosis such as "dystrophy of the hair and nails," "imperfect development of skin, hair, and teeth," "defect of hair and teeth" and other classifications. A better and more generally used term is "congenital ectodermal defect." None of these terms indicate the three salient factors of etiologic importance: that (1) the tissues affected are principally of ectodermal origin, (2) the defects are developmental anomalies and (3) the hereditary tendencies are strongly developed. I am therefore suggesting the term "hereditary ectodermal dysplasia" as descriptive of these essential features of the condition.

It is difficult to believe that there is any important etiologic distinction between the cases characterized chiefly by absence of sweat glands and those showing a smaller number of defects. In two cases reported patients displayed almost identical anomalies of the hair and teeth. One had malformed nails and normal sweat glands; the other presented normal nails and an absence of perspiration. Oliver and Gilbert [11]

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7. Tendlau, B.: Ueber angeborene und erworbene atrophia cutis idiopathica, Virchows Arch. f. path. Anat. **167**:465, 1902.

8. Loewy, A., and Wechselmann, W.: Zur Physiologie und Pathologie des Wasserwechsels und der Wärmeregulation seitens des Hautorganes, Virchows Arch. f. path. Anat. **206**:79, 1911 (complete description with illustrations). Wechselmann, W., and Loewy, A.: Untersuchungen an drei blutsverwandten Personen mit ektodermalen Hemmungsbildungen, besonders des Hautdrüsensystems, Berl. klin. Wchnschr. **48**:1369, 1911.

9. Christ, J.: Ueber die kongenitalen ektodermalen Defekte und ihre Beziehungen zu einander, Arch. f. Dermat. u. Syph. **116**:685, 1913.

10. Strandberg, J.: Nord. med. Ark. **51**:1, 1918.

11. Oliver, E. A., and Gilbert, N. C.: Congenital Alopecia, Arch. Dermat. & Syph. **13**:359 (March) 1926.

recently reported two cases in brothers who presented hypotrichosis and deficient perspiration, but in whom the teeth and nails were normal. A sharp division would therefore be unwise, but I agree with Goeckermann and with MacKee and Andrews that a subclassification may be helpful. I prefer, however, to substitute for such adjectives as "high-grade" and "major," a term descriptive of the cardinal symptom of the group, namely, inability to perspire. I shall, therefore, designate this special group as the anhidrotic type of hereditary ectodermal dysplasia.

SIGNS AND SYMPTOMS

In surveying the entire group of hereditary ectodermal dysplasia there are a number of defects that have been described both alone and in combination with other defects. These may be conveniently classified by considering the various tissues of ectodermal origin and pointing out the malformations and symptoms that may occur.

(*A*) *The Skin.*—The majority of the anomalies of the skin to be found in this group of cases do not occur alone, but in combination with each other. In general, a patient who can perspire presents a normal skin in other respects. Moreover, when the skin is involved the hair, teeth and mucous membranes of the rhinopharynx are nearly always affected also. It is this pronounced tendency of a certain number of the anomalies to occur always together which serves to mark out the anhidrotic group as a seemingly separate entity.

(1) Character of the skin. Wilson, who made the microscopic study of the tissues obtained from the autopsy on Thurnam's patient, begins his description by saying, "The peculiarities of the portions of skin sent to me are their whiteness, thinness and softness, and the tenuity of, and absence of pigment in, the epiderma." Goeckermann described the skin of his patient as being "exceptionally fair, smooth, thin, pliable and dry and showed the superficial veins plainly." In other reported cases, the descriptions are similar. The achromic condition of the skin, marked enough in Strandberg's case to cause him to use the descriptive phrase "white as alabaster" may be mentioned specifically, as this feature was absent in my patient (H. C.). Microscopic studies on tissue obtained at biopsy have been reported by Loewy and Wechselmann, Strandberg, Goeckermann and MacKee and Andrews. With the exception of the glands, Goeckermann described the skin as normal. In other cases the epidermis has been thin and revealed other evidences of defective development.

(2) Absence of sweat glands. As has been mentioned, inability to perspire is the principle defect that marks the anhidrotic group of cases. In all of the reported cases the defect has been complete, no response of the sweat glands being noted even after the administration of sudorific drugs. From the standpoint of the patient's comfort this

inability to perspire is the most important of all the anomalies, as it usually necessitates alterations in the whole manner of living. These people are extremely intolerant of heat. When working in the field in the sun Guilford's patient found it necessary to engage a boy to carry buckets of water which were poured over his clothing. If for any reason the water was slow in arriving, he frequently collapsed from the heat. Tendlau's patient was able to eat only cold foods in the summer, as hot dishes produced fever. When he was exposed to the summer sun, an axillary temperature of more than 104 F. had been observed. The patient (H. C.) whose case is reported in this paper carried a wet handkerchief with him in hot weather with which he mopped his head from time to time. In the several biopsies previously referred to, complete absence of the sweat glands was indicated.

The absence of sweat glands has induced several investigators, chiefly Tendlau and Loewy, to utilize patients of this type in studying the rôle of the sweat glands in controlling loss of water through the skin. Their results indicate that a person with total absence of sweat glands eliminates a normal amount of water through the skin when at rest in a cool atmosphere, and that therefore sensible perspiration, which represents the secretion of the sudoriparous glands, is merely an important emergency secretion.

(3) Absence or faulty development of sebaceous glands. This defect in association with absence of the sweat glands is responsible for the dryness of the skin which patients belonging to the anhidrotic group have regularly exhibited. In the biopsy performed by MacKee and Andrews, sebaceous glands in tissue from the forearm and in the tissue from the face, though normal numerically, were rudimentary.

(4) Papular lesions on the face. Papular lesions on the face in patients belonging to the anhidrotic group have been mentioned by a number of observers. The type and distribution has varied, but in general the descriptions resemble that given for my first case. MacKee and Andrews stated: "Histologically lesions appeared to be the result of large, superficially placed, degenerated sebaceous glands, together with hyperkeratotic, dilated, follicular orifices, and surrounding acanthosis." It is of interest that in my first case the papular lesions were observed and their distribution on the face marked when the patient was only 9 weeks of age.

(5) Epidermolysis bullosa. Epidermolysis bullosa has thus far not been described in patients of the anhidrotic type. However, in a number of instances it has occurred in association with congenital alopecia and at least once with defective hair, teeth and nails. A familial tendency has also been noted.[12]

12. Wende, G. W.; Guy, W. H., and Sweitzer, S. E., in discussion on paper by Oliver and Gilbert (footnote 11).

(*B*) *Epidermal Appendages.*—Defects of the hair and teeth occur regularly in the anhidrotic group, not infrequently anomalies of the nails are also present. Similar malformations in various combinations occur much more frequently in patients who do not present all of the cardinal signs of the group.

(1) Hair. Complete alopecia at birth has been noted in a number of instances, but to my knowledge a complete permanent alopecia has not been described. The deficiency of hair does not occur in the form of a patchy alopecia, but instead the hairs are diffusely scattered over the head and much decreased in numbers. The hair is always described as fine in texture. Occasionally, a few normally coarse hairs have been interspersed.[13] The pigment is usually deficient, the growth slow and the maximum length much below the normal. Sometimes they seem insecurely rooted and can easily be pulled out.[14] The defective growth of hair is usually evident in other parts of the body. Absence of lanugo hair over the body is the rule. Eyebrows and eyelashes may be absent [15] or merely thinned in numbers. In both of my cases and in the case reported by MacKee and Andrews only the medial portion of the eyebrows was present. The axillary and pubic hair is affected less frequently though it may be absent. When present, it usually does not show the achromia exhibited by the hair on the head. In several instances in male patients the crines have been of the female type.[16] Strangely enough, nearly all of the men have been able to grow mustaches.

(2) Teeth. Complete absence of all of the teeth, although exceedingly rare, has been reported in several instances. The patients described by Guilford and by Strandberg were edentulous. On the other hand, patients with malformations of the hair and nails frequently display normal dentition, or the dental anomaly may be merely a tendency to early decay. Oliver and Gilbert's patients who exhibited combined defects of the hair and sweat glands had essentially normal teeth. More frequently, however, the teeth are markedly decreased in numbers, and apparently the lower jaw is much more apt to be edentulous than the upper.[17] When teeth are present, those in the front of the mouth are usually of abnormal configuration; molar teeth are of normal form. Thurnam's patient had only four molar teeth which were pronounced

13. Eisenstaedt, J. S.: Three Cases of Familial Dystrophy of the Hair and Nails, J. A. M. A. **60**:27 (Jan. 4) 1913.

14. White, C. J.: Dystrophia unguium et pilorum hereditaria, J. Cutan. & Gen. Urin. Dis. **14**:220, 1896.

15. Jacobsen, A. W.: Hereditary Dystrophy of the Hair and Nails, J. A. M. A. **90**:686 (March 3) 1928.

16. MacKee and Andrews (footnote 2). Strandberg (footnote 10).

17. Goeckermann (footnote 1). Thurnam (footnote 3). Ascher (footnote 6). Tendlau (footnote 7). Christ (footnote 9).

normal by his dentist. My second patient had four normal first molars, my first patient a single right rear molar of normal form. On the other hand, the teeth in the front of the mouth were frequently misshapen. In their case, MacKee and Andrews described the upper incisors as being "somewhat gimlet shaped." In both of my patients all of the teeth in the front of the mouth were pointed so as to resemble canines; there were none with flat cutting edges. A decision as to whether the more lateral of the teeth should be classed as canines or incisors is therefore impossible. In Ascher's two patients only three and two upper incisors were present. These teeth were described by Loewy and Wechselmann as being bottle-shaped. The authors have given illustrations of plaster models of the jaws of both patients; the illustrations show the teeth to be of exactly the same type as those exhibited by my patients. Teeth of this kind are nearly always inclined forward in the mouth. I was much interested to discover an article by Cole[18] describing a combined defect of hair and teeth occurring in cattle. The incisor teeth of these animals (confined to the lower jaw in cattle), instead of being sharp and flat, were conically blunt and too few in number (two on each side instead of four). A published illustration of these teeth shows that they resemble strikingly those seen in the mouths of my patients. It would seem, therefore, that the cone-shaped incisor tooth represents a special form of anomaly particularly prone to occur in this group of cases.

(3) Nails. In the anhidrotic group, the nails are more often normal than deformed. In my case of this type the nails were normal. Anomalies, however, were present in the cases reported by Christ, Strandberg, Goeckermann, and MacKee and Andrews. On the other hand, dystrophy of the hair is more often associated with changes in the nails than with dental anomalies. When the finger-nails are involved the same type of condition is usually exhibited by the toe-nails, though this did not occur in the case of MacKee and Andrews. Various types of alterations are encountered; perhaps the most common of these is a tendency to horny hypertrophy.[19] This hypertrophy is least evident at the base and becomes more marked distally, causing the nails to project at an angle from the nail-bed. Such nails are usually extremely

18. Cole, L. J.: A Defect of the Hair and Teeth in Cattle, Probably Hereditary, J. Hered. **10**:303, 1919.

19. Eisenstaedt (footnote 13). White (footnote 14). Jacobsen (footnote 15). Murray, F. A.: Congenital Anomalies of the Nails: Four Cases of Hereditary Hypertrophy of the Nail-Bed Associated with a History of Erupted Teeth at Birth, Brit. J. Dermat. **33**:409, 1921. Nicolle, G., and Halipré, A.: Sur un cas de dystrophie unguéale et piliare familiale, Ann. de dermat. et syph. **6**:675, 1895; Maladie familiale caractérisée par des alterations des cheveux et des ongles, ibid., 1895, p. 804.

brittle, easily traumatized and are singularly susceptible to paronychia. It is significant, however, that none of the patients in the anhidrotic group have shown this type of deformity of the nails. In Goeckermann's patient the nails exhibited uniform, fine longitudinal furrows. The patient of MacKee and Andrews was described as having finger-nails which were flat with free lateral margins. The nails in my second patient were flat or slightly concave instead of convex, the malformation being most conspicuous at the nail-bed, that is, they belonged to the type that have been described as "spoon nails."

(4) Mammae. In Tendlau's patient who belonged to the anhidrotic group the mammary glands were absent. Hutchinson [20] also reported the case of a boy, aged 3½, who presented a deficiency of hair and abnormal finger-nails associated with absence of the nipples. In Ascher's second case (F. K.), the nipples were flat and the mammae apparently absent. In neither of my patients was any defect in the mammary gland noted.

(*C*) *Mucous Membranes of Mouth and Nose.*—So far as I am aware, the alterations of the mucous membranes commonly associated with other ectodermal defects have been described only in the anhidrotic group. In this special group, however, the changes are almost always found, the case of MacKee and Andrews being a distinct exception. The alteration is usually described as an atrophic rhinitis. Atrophy of the mucous membranes of the pharynx and larynx have been described, the latter producing a distinct hoarseness.[1] Guilford did not give any description of the membranes, but mentioned the fact that his patient was lacking in the sense of smell and almost devoid of any sense of taste. It should be emphasized, however, that the primary condition of the mucous membranes in these patients must be one of lack of development rather than the result of infection. In the first case reported by me, the presence of dry snuffles and hoarseness of the cry were observed when the patient was first examined at the age of 9 weeks.

Poor definition of the vermilion border of the lips was first noted by Goeckermann and later by MacKee and Andrews. This condition was present in my second case and absent in the first.

(*D*) *Nervous System.*—In view of the ectodermal origin of the nervous system it seems extremely important to know whether the mental inferiority which a number of patients have exhibited is the result of the same germinal mutation responsible for the other ectodermal defects. Because of the extreme frequency of retarded mental development as a condition per se, one is not convinced of the identity of etiology in these cases. It is not necessary to enumerate the many cases

20. Hutchinson, J.: Congenital Absence of Hair and Mammary Glands, Proc. Roy. M. & Chir. Soc. **69**:473, 1886.

in which the mental development has been unimpaired. The two cases I have reported exemplify this. However, Tendlau's patient was of inferior mentality, and in both of the cases of Loewy and Wechselmann and in Christ's case the mentality was also impaired. The patient described by Thurnam was normal mentally, but a sister, an uncle and a cousin on the father's side had died insane. Barrett [21] reported observations on a family in which among sixty-one members belonging to six generations fourteen showed anomalies of the hair and nails. Many members of this family presented constitutional nervous disorders (epilepsy, tics, hysteria, feeblemindedness and enuresis), but the inheritance of these characteristics did not run parallel to that of the changes in the hair and nails. If called on to offer a prognosis in regard to mental development in a case of hereditary ectodermal dysplasia in an infant or young child, I would feel that the outlook was good unless an inherited nervous disorder already existed in the family, and even if such a history did exist, it seems not improbable that the child might escape.

(E) Organs of Special Sense Such as the Eye and Ear.—In most of the reported cases of hereditary ectodermal dysplasia there are no notes indicating involvement of the organs of special sense. One is doubtful whether any important relation exists. Several features have been described, however, and may be mentioned here. In each of the two brothers described by Ascher and by Wechselmann and Loewy the right ear was of different conformation from the left. The ear was pointed at the top (Satyrohr), the cartilages hyperplastic and separated by a deep sulcus. The ear stood out at an angle from the head, and the auricle itself was curved forward. MacKee and Andrews reported in their case that the lobes of the ears were small and attached to the cheeks. In my first case the auricles were small and stood out obliquely from the head, but as this observation was merely an exaggerated expression of a familial tendency, I am inclined to minimize its importance. Papastratigakis [22] described a patient in whom cataracts, total alopecia and alterations in the nails occurred together, and Tomkinson [23] called attention to a familial relation between alopecia areata and strabismus. The cases described by Tomkinson do not much resemble those being considered here. The alterations in the senses of taste and smell which several patients in the anhidrotic group have exhibited are in all probability secondary to the atrophic condition of the mucous membranes.

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21. Barrett, A. M.: Hereditary Occurrence of Hypothyroidism with Dystrophies of the Nails and Hair, Arch. Neurol. & Psychiat. **2**:628 (Dec.) 1919.

22. Papastratigakis, C.: Un nouveau syndrome dystrophique juvenile, alopécie totale associée a la cataracte et à des alterations onguéales, Paris méd. **45**:475, 1922.

23. Tomkinson, J. G.: Alopecia Areata and Strabismus: Familial Groups, Brit. M. J. **2**:518, 1924.

(*F*) *Alterations of Nonectodermal Origin.*—Whereas, nearly all of the malformations considered have occurred in tissues that developed from ectoderm, nevertheless there are a few changes, of remarkable constancy in the anhidrotic group, in which the origin cannot be traced to a condition of this germ layer. Chief among these is the character of the bones of the skull; because of their position the prominence of the supraorbital ridges has received the most attention. But the change is more general than this and probably may include all of the cranial bones. The observations in my patient (H. C.) are illustrative of this. In the biopsy performed on his patient, Thurnam noted that all of the cranial bones were thickened. The flattening of the nasal bridge, sometimes amounting to a recession and producing a real saddle nose, has been a regular observation in these cases. The relation of these bony changes to the multiple ectodermal defects is not clear. One may suspect that in some unexplained way the former are secondary to the latter, but one does not feel competent to suggest an adequate explanation.

Thick, muscular, protrusive and everted lips have been observed regularly in this same group. Guilford supposed that this feature represented a physiologic hypertrophy, the function of the teeth being taken over by the lips in the seizure of food. My first patient assured me that his lips have nothing to do with the manner in which he takes food; for this purpose the gums replace his teeth. Even so it is true that the lack of teeth brings the jaws closer together, so that there is less room for normal development of the lips. This anatomic condition of his jaws may be responsible for the eversion and hypertrophy of the patient's lips. It is of interest, however, that when he was examined at the age of 9 weeks the epithelium of the lips appeared thickened. It would seem that this feature also may find its explanation in changes brought about in early embryonic life.

ETIOLOGY

Syphilis.—In the first case reported by me the history of early desquamation of the palms and soles, the alopecia which included the eyebrows, the early development of dry snuffles and the deformity of the nasal bridge, the hoarseness and the unusual papular lesions on the face combined to render a diagnosis of congenital syphilis most probable. Nevertheless, there were no lesions that were obviously syphilitic and no family history suggestive of parental infection. Moreover, the results of three Wassermann tests taken over a wide period of time were all negative. The remarkable disturbance of dentition could suggest syphilis only in so far as it is known that this disease can modify the form of the teeth, but there is not the remotest resemblance between the Hutchinson teeth of congenital syphilis and those exhibited by my patient. I would regard syphilis as an exceedingly improbable etiologic

factor, even if another likely cause was not apparent. A similar suspicion of syphilis has been aroused in a number of the reported cases of the anhidrotic type of ectodermal dysplasia. Some of these patients have been given antisyphilitic treatment, but it is noteworthy that not one of them has had a positive Wassermann reaction. In the case reported by MacKee and Andrews the resemblance of the patient's symptoms to those produced by syphilis was further increased by the presence of rhagades-like radiating scars at the corners of the mouth. However, in view of the obvious ectodermal origin of nearly all of the affected tissues it is apparent, as Goeckermann has stated, that to suppose that *Spirochacta pallida* was the responsible agent, it would be necessary to assume that the injurious influence had been suddenly exerted at the time of the third or the fourth month of embryonal existence and had then rapidly subsided. Such a supposition is rendered further unlikely by the known hereditary and familial features of the condition.

Endocrine Disturbances.—As there is no definite knowledge concerning the possible function of hormones in regulating the processes of intra-uterine development, and since it is conceivable that a primary endocrine dysfunction might be a factor of importance in the production of various multiple congenital anomalies, it is not possible to dismiss these glands entirely from consideration. In the specific case of the ectodermal dysplasias, since it is known that the anomalies may be transmitted through the male, one would be forced to assume that the endocrine influence could act on the original germ cell in such a manner as to influence its entire subsequent development, an assumption both unlikely and unwarranted by any known biologic analogies.

There are, however, several symptoms exhibited by these patients which have led more directly to the suspicion of endocrine disturbance. It is known that dysfunction of the thyroid as seen in the cretin may lead to abnormal development of the hair and lessen the secretion of the sweat and sebaceous glands. In the second of my cases there was a persistent elevation of the basal metabolism, and in the case reported by Jacobsen the basal metabolic rate was plus 23 per cent. Barrett noted an increased dextrose tolerance in one of his patients. In his case, Thurnam found an enlarged thyroid at autopsy. In several instances, as in my first case, physical examination has shown slight enlargement of this gland. These observations, however, have not been consistent and probably do not bear any causal relationship to the associated defects. In my first case the basal metabolic rate was 10 per cent below normal; in the case of Oliver and Gilbert it was only plus 9.6 per cent. Barrett reported that one of his patients improved when treated with thyroid extract, but that the other responded very little.

The small sella turcica demonstrated by the roentgen examination in my first patient might suggest pituitary hypoplasia. I am not sure of

the relation of this observation to the other anomalies, but prefer to regard it as the result of the same process that altered the conformation of the visible skull bones. In my second case and in the case of Oliver and Gilbert the sellas were normal.

Infection.—This etiologic agent is mentioned only to say that in all cases in which the hair and nails have been searched for possible mycotic organisms the search has been fruitless.

Heredity.—It is now well established that the types of defects considered frequently occur in a hereditary manner. From the standpoint

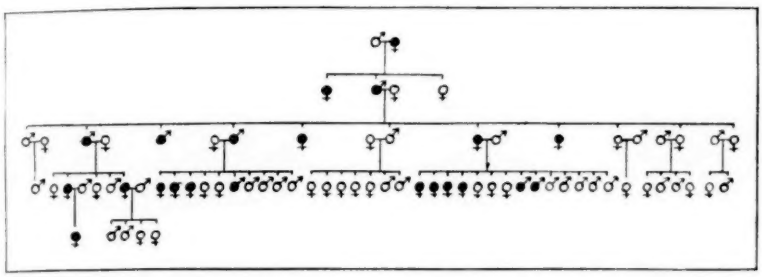

Fig. 5.—Geneologic tree of family reported by Jacobsen, the affected members of which showed defects of the hair and nails. The anomalies have been transmitted by both males and females, but in no case has an unaffected person been able to transmit them.

	NORMAL	AFFECTED
MALE	♂	●
FEMALE	♀	●
SEX UNKNOWN	○	●

Fig. 6.—Explanation of symbols in geneologic trees.

of the genetic laws governing the mode of transmission of these anomalies, however, the data available in the literature are conflicting. To attempt a complete explanation would lead one far into the field of speculation. I must content myself, in the main, with presenting what data there are.

Jacobsen [15] recently reported data concerning a family in which associated defects of the hair and nails were present in twenty-two of sixty-four members in five generations. He also reproduced in his article the pedigrees of four additional families collected from the literature in which similar defects could be traced through a number of

generations. I am giving here the family tree prepared by Jacobsen. The others are similar. From a study of these pedigrees, Jacobsen concluded that the transmission was mendelian, nonsex-linked in character. That is, both males and females were capable of transmitting the anomalies; in either case both male and female children might be affected, but a member of the family who was normal could not transmit them. In a recent dental journal, Gardner [24] has given the pedigree of a family characterized by a large number of congenitally missing teeth. In this family of nineteen persons in six generations, about whom data were available, twelve were affected. From a study of his chart, the same conclusion regarding the manner of transmission can be drawn.

When attention is directed to the anhidrotic group of ectodermal dysplasias, the extreme rarity of the cases renders long pedigrees unavailable. Nevertheless, the little data that do exist are of the greatest interest. The family tree originally published by Ascher and later copied by Loewy and Wechselmann is the most complete in the literature. From the data given in their chart and from the descriptive matter in

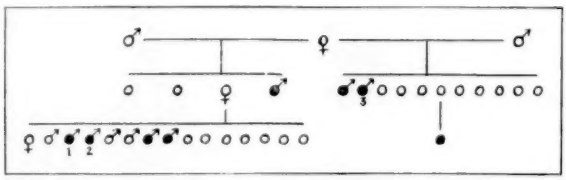

Fig. 7.—Geneologic tree of family investigated by Ascher. Patients 1, 2 and 3 are well described in the literature. The maternal grandmother of Ascher's two patients was married twice. From each marriage there were descendants who showed the same anomalies. A stepsister of this maternal grandmother is also reported as having a son who was similarly affected. Thus, there were nine persons in this family known to have shown the same defects. The sex of eight of these is stated; all were males. In each case the inheritance appears to have been through the female.

the text I have constructed a pedigree which is given here. Nine members of this family were known to have exhibited the anomalies. Three have been excellently described (two by Ascher, one by Tendlau; all three redescribed by Loewy and Wechselmann). Eight of these affected persons were males; the sex of the ninth is not stated. There were no known cases in females, but in every case inheritance of the anomalies was through the female. In this family then the inheritance appears to have been strictly sex-linked, and analogous to that which occurs in hemophilia and color blindness. Other complete pedigrees of families presenting this form of ectodermal dysplasia do not exist, but most of

24. Gardner, T. A.: Six Generations of Congenitally Missing Teeth, Dental Cosmos, **69**:1041, 1927.

the available fragments of family histories are in accord with the sex-linked manner of inheritance. The patient described by Thurnam had a first cousin on his mother's side with identical anomalies. Both were males. Guilford's patient, a man, had a mother who was normal, but her brother lacked hair and teeth. Whether he was also unable to perspire is not stated. Christ's patient, also a man, had a younger brother and a first cousin on his maternal side who were similarly affected. My patient (H. C.), a boy, has one normal brother, but another brother, now dead, was affected as he is. I was unable to trace the anomalies further in his family. The patients of Strandberg and of MacKee and Andrews were both males, but pertinent family histories could not be elicited. Of greatest interest, however, is a report by Thadani [25] of a type of men occurring in the Hindu Amil community of Hyderabad Sind, a town in India. These men are characterized by an absence of teeth, a bald head and by an extreme sensitiveness to heat. Although meager, this description is probably sufficient to identify them as persons afflicted with the anhidrotic form of ectodermal dysplasia. Thadani's publication was in the nature of a preliminary report. Actual pedigrees were not given, but the author stated that the inheritance has been strictly sex-linked.

Were no more to be said, it would seem that the inheritance data just given would be in themselves sufficient to separate the anhidrotic from other forms of ectodermal dysplasia. On the clinical side several features might be cited as favoring such a division. In none of the families whose pedigrees were collected by Jacobsen did anomalies of the teeth or sweat glands occur. The prevailing type of nail deformity in these families was a horny hypertrophy, a type of malformation not recorded in the anhidrotic group. Gardner's report of the hereditary transmission of missing teeth does not contain any reference to cone-shaped incisors, a type of anomaly so regularly found in anhidrotic cases. On the other hand, straight, fine, sparse, dry and achromic hair was a constant observation in both groups. Moreover, in my second case in which the sweat glands were normal, typical cone-shaped incisors of the same kind found in the anhidrotic type were present, and the family history suggested strongly that the defect had been transmitted through the male. It is of interest also that this type of teeth occurred in the herd of cattle described by Cole with defective hair and teeth. In this herd, there were five affected calves sired by an affected bull. The sex of the calves was not stated, but the anomaly was transmitted through the male.

One fact of the greatest importance remains to be stated, a fact which does much to weaken the full acceptance of the sex-linked

25. Thadani, K. I.: A Toothless Type of Man. The "Bhudas" of India—A Case of Sex-Linked Inheritance, J. Hered. **12**:87, 1921.

character of the inheritance in the anhidrotic group. This fact is that the patient described by Goeckermann was of the female sex. Moreover, although not described in detail, the patient cited by Williams in the discussion following the presentation of Thurnam's patient was also a woman. Also, the maternal grandmother of the patient reported by Guilford lacked both hair and teeth, although I do not know whether she was also unable to perspire. If the undescribed members of this family did belong to the anhidrotic group, the inheritance would be most unusual in that the anomalies after first appearing in the female were thereafter transmitted in an apparently sex-linked manner. One son of this grandmother lacked hair and teeth, and a daughter who was normal was the mother of Guilford's patient. Although the reported cases of this type of defect in women are too few to allow the drawing of any conclusions, it has interested me to note that there does not exist any record of a female who has apparently acquired her defects through inheritance. The only female patient to be adequately described is that of Goeckermann, and in this instance a pertinent family history could not be elicited. Even more than this, there does not exist an example of an affected male who has transmitted his anomalies to his male grandchildren through a normal daughter. Obviously a more thorough analysis cannot be made until more and longer pedigrees have been assembled. Thus far, the inheritance of anomalies as a group has been considered without considering the possibility that the number of ectodermal tissues involved may show variations within members of the same family. Such variations are recorded in all types of ectodermal dysplasias and serve to make less clear a distinction between possible different forms. In the families whose pedigrees were collected by Jacobsen the number and form of the anomalies were in general singularly constant; even here it may be noted that in the pedigree of the family reported by White there were some persons who showed changes in the nails but who had normal hair, while in others both were involved. Barrett also had recorded that the various members of the family concerning whom data were reported by him showed many different degrees of alopecia. In the second case that I have reported the patient did not have any relatives with anomalies as extensive as hers, but her father had an imperfectly formed tooth, and two of his uncles had missing teeth. Moreover, Guilford's patient had several brothers and sisters and several children who were normal in every way except that certain teeth were missing.

In reviewing all of these heterogeneous data concerning the form of inheritance displayed by ectodermal dysplasia, it is difficult to form any definite conclusions. In a broad way one can say that the cases tend to fall into two groups: in the one the inheritance is dominant nonsex-linked, in the other it is sex-linked. The fact that some of the anomalies may be identical in the two groups is in accord with the fact

now well established by breeding experiments that totally different genes may be concerned with the production of identical adult characters. Whether in each group it is possible to associate all of the anomalies with the modification or mutation of a single gene within a single chromosome seems doubtful. In the families whose records were collected by Jacobsen, only the hair and nails were affected, and the two defects nearly always appeared together. In the few instances in which the nails alone were affected, the persons were able to transmit both anomalies. In this case, then, a single mutant gene within an autosome could account for all the anomalies. In the sex-linked group, however, there existed more of a tendency for some of the anomalies to be transmitted in the absence of others. Here it seems likely that several genes are involved, but that the principal gene is located within the sex chromosome and that in general it can influence the expression even of genes which may be located within other chromosomes. Thus anhidrosis may be one of the characters represented by the principal gene. This gene is probably able to exercise some influence on dentition as well, but it seems likely that other normally recessive mutant genes located in other chromosomes are also concerned in the production of the tooth defects, and that their dominance relation may be altered by the presence of the principal gene. Examples are known to geneticists in which a character X, normally recessive, will behave as a dominant in the presence of a different character Y. Thus, in general, the transmission will appear sex-linked. If the gene or genes concerned with the dental anomaly are transmitted alone, the dentition will probably be normal, as these genes are recessive; but if the same type of mutant genes are present in both parents, the children of either sex may show dental defects even in the absence of anhidrosis.

An adequate explanation for the occurrence of the anhidrotic syndrome in the female is not possible. When dealing experimentally with other sex-linked characteristics it is possible to obtain them in the female by mating an affected male with a female carrier. In the case under consideration the extreme rarity of the condition would render such a combination most improbable. Furthermore, it is known that both parents of Goeckermann's patient were normal. In rare instances geneticists are able to observe the occurrence of sex-linked characters in the female when the possibility of this type of combination is excluded. Here the phenomenon is attributed to an occasional normal distribution of the chromosomes when the germ cells are formed, a process which is referred to as the phenomenon of nondisjunction. Experimentally, the phenomenon is observed in such a small percentage of cases that it cannot be said to furnish a satisfactory explanation in the present case.

One other explanation may be offered which although somewhat speculative is at least in accord with my data. The modern geneticist no

longer believes that the genes are immutable entities, but rather that the basis of heritable variation lies in infrequent sudden changes in individual genes. Moreover, it is certain that there are types of alterations or mutations to which certain genes are particularly susceptible in just the same way as the fully developed person is subject to certain well recognized diseases. To suppose that all cases of hereditary ectodermal dysplasia in the human being are traceable to a common ancestor would be incredible. Cases of the anhidrotic type have now been reported from America, England, Germany and Sweden. Two patients were Jews. If Thadani's report is correct, the condition is fairly frequent in India. It would thus seem that the various ectodermal defects may be the result of some mutation of the genes which occurs not by accident, but as the occasional expression of a suppressed tendency to change inherent in the make-up of the genes themselves. If a condition of this type has its origin as it must in a genetic mutation, it seems possible that the mutation itself may occur regardless of sex and that in the beginning either males or females may be affected. Thereafter, the transmission would be sex-linked and the anomalies appear only in the male. This theory is in accord with the fact that in neither of the female patients described in the literature is there a record of antecedents similarly affected and harmonizes with the pedigree given by Guilford for the family of his patient in which an affected woman had one affected son and a normal daughter who was the mother of Guilford's patient.

DIAGNOSIS

When several or more of the ectodermal tissues are involved or when a definite hereditary factor can be shown, it scarcely seems possible that a mistake in diagnosis can occur. In isolated cases in which the hair and nails only are affected, it may be desirable to exclude by culture the presence of mycotic organisms. In the anhidrotic group the possibility of confusion with congenital syphilis has already been mentioned. But when the ectodermal origin of all the affected tissues has been appreciated, there should be no difficulty, even if the patient was also affected with syphilis.

To one condition, however, I wish to draw special attention, namely, to the condition described by Hastings Gilford [26] in 1904, as progeria or premature senility. I am moved to do this because two competent observers who saw my two patients at different times were impressed by the appearance of premature old age resulting from the loss of hair and teeth and were led to make an incorrect diagnosis. In describing his case of ectodermal dysplasia, Hutchinson [20] said that the boy, aged 3½ years, presented a peculiar withered or old-mannish look. But one

26. Gilford, H.: Progeria; A Form of Senilism, Practitioner **73**:188, 1904.

has only to read the description of the two remarkable cases reported by Gilford to appreciate how superficial is the resemblance to ectodermal dysplasia. In these patients, in addition to early loss of hair and abnormalities of dentition, there were evidences of rapidly advancing arteriosclerosis and of the physical and mental infirmities of age, and death occurred before the age of 20 years. Each time the condition was associated with ateliosis, an association which in itself should be sufficient to distinguish it from hereditary ectodermal dysplasia. Moreover, there is no reason to believe that ectodermal dysplasia in any way shortens the span of life.

SUMMARY

1. Two patients are described, both of whom exhibited multiple congenital anomalies of tissues arising principally from the ectoderm. Both patients showed defective development of the hair and teeth, unusual conformation of the skull and thick prominent lips. In both cases, histories were obtained indicating that heredity was a factor in the production of the anomalies. In addition, the first patient presented a smooth, dry, glossy skin with apparent total absence of sweat and sebaceous glands, papular lesions on the face, malformation of the nose, an atrophic rhinopharyngolaryngitis and heat intolerance. These observations were absent in the second patient, who showed, in addition, defectively formed nails, poor definition of the vermilion border of the lips and an elevated basal metabolic rate.

2. A discussion is given of the various reported types of congenital ectodermal defects. Among these, a rare type characterized by total absence of sweat glands in regular association with other anomalies is particularly described. Only ten cases have been previously reported, the first of the two cases reported by me being the eleventh. A complete review of the literature connected with this type is given.

3. An attempt is made to provide a satisfactory diagnostic term under which the various congenital anomalies of ectodermal origin may be classified. The term suggested is "hereditary ectodermal dysplasia." It is further suggested that the particular group characterized principally by absence of sweat glands be designed as the "anhidrotic type" of hereditary ectodermal dysplasia.

4. The varied manifestations of hereditary ectodermal dysplasia are discussed in detail and in relation to the several tissues developed from ectoderm. The importance of the absence of sweat glands from the standpoint of the intolerance to heat displayed by patients so afflicted is particularly emphasized. Special attention is drawn to the cone-shaped incisor tooth, a form of anomaly particularly prone to occur in patients of this group.

5. Mention is made of important researches into the nature of sensible and insensible perspiration made possible by the utilization of patients without sweat glands.

6. In discussing the etiology of these conditions, syphilis, infection, endocrine disturbance and heredity are considered. Syphilis and infection are mentioned merely to be excluded. The possibility that an endocrine disturbance may be an important etiologic factor is thought improbable.

7. The manner of hereditary transmission of ectodermal dysplasia is discussed in detail. It is shown that in some instances the inheritance is dominant nonsex-linked, while in others it is apparently sex-linked. An attempt is made to explain these variations.

8. It is suggested that the various ectodermal anomalies may arise as the result of a genetic mutation which occurs, not by accident, but as the occasional expression of a suppressed tendency to change inherent in the make-up of the genes themselves.

9. In discussing the differential diagnosis, attention is called to the possibility of confusion with the condition described by Gilford as progeria or premature senility.

THE INSENSIBLE PERSPIRATION IN INFANCY AND IN CHILDHOOD

I. ITS CONSTANCY IN INFANTS UNDER STANDARD CONDITIONS AND THE EFFECT OF VARIOUS PHYSIOLOGIC FACTORS *

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AND

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NEW YORK

Previous workers who have used the balance to measure the insensible perspiration of infants have not adequately controlled the technic of the measurements or fully recognized the influence of extraneous factors. One group of observers [1] held that the insensible perspiration, measured by the method of weighings, varies from day to day, even under the same conditions; whereas another group [2] maintained that the rate is intrinsically constant and that the variations so frequently reported arise from extraneous factors not carefully controlled. Studies with the calorimeter and the respiration chamber offer presumptive evidence in favor of the latter view. They show a striking correlation in adults,[3] children [4] and infants [5] between the production of heat and the vaporization of water through the skin and the lungs under basal and other conditions.

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* Submitted for publication, Oct. 10, 1928.

* From the Department of Pediatrics, Cornell University Medical College, and the New York Nursery and Child's Hospital.

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2. Meyer, J.: La perspiration de l'eau chez le nourrisson, Rev. franç. de pédiat. **1**:409, 1925; La broncho-pneumonie du nourrisson. Étude physio-pathologique et thérapeutique, Paris, Amédée Le Grand, 1923. Baumecker, W., and Schonthal, L.: Ueber Wasserversuch am Säugling bei Konzentrierter Ernahrung, Ztschr. f. Kinderh. **40**:211, 1926. De Rudder: Der Perspiratio insensibilis beim Säugling: I. Zür Physiologie der Perspiratio insensibilis beim Säugling, ibid. **45**: 404 (March) 1928.

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5. Levine, S. Z., and Wilson, J. R.: The Respiratory Metabolism in Infancy and in Childhood: VII. Elimination of Water Through the Skin and Respiratory Passages of Infants, Am. J. Dis. Child. **35**:54 (Jan.) 1928.

The meager and conflicting evidence available in the literature prompted these preliminary studies of the various physiologic factors affecting the rate of insensible loss in infants. Such studies were indispensable at the outset for defining, if possible, the optimal environmental conditions for securing basal measurements with the balance and for determining the constancy of the basal rate under these standard conditions. The present paper reports the results of these studies. The basal figures obtained in a representative group of infants under the standard conditions will be presented in another communication.[6]

APPARATUS AND METHODS

The room in which the measurements were made was fully described in a previous paper.[7] The presence of two windows, a door and a heater made possible a wide range of room temperatures in the different observations and uniform temperatures during individual observations. In the latter, maximal variations rarely exceeded 1 C. Diurnal fluctuations in the relative humidity of the air in the room were insignificant and never exceeded 5 per cent in individual experiments. Readings of wet and dry bulb temperatures of the air were made at intervals of approximately thirty minutes during experiments, and the effective temperature[8] and the relative humidity were estimated from standard tables.

A delicate balance with a capacity of 10 Kg. and with an accuracy of 20 mg. was employed to measure the insensible perspiration[9] by the method of successive weighings. One full swing of the indicator required about thirty seconds, during which the subject might lose a maximum of 50 mg. in weight, but the resultant error never exceeded 2 per cent and averaged 1 per cent.

During weighings, the subject lay on a specially constructed bed suspended from the balance by flexible brass chains. The bed consisted of a frame of hollow brass piping about one-half inch (1.27 cm.) in diameter, across which was strung a thin fish net with a 1 inch (2.5 cm.) mesh. A narrow pad completely enclosed in a rubber jacket covered the net and served as a mattress. The net and the pad extended only partially across the lower half of the bed and left a central gap for the unobstructed passage of a rubber tube that led from the genitalia into a basin layered with oil and attached to the frame of the bed. Another larger basin, also layered with oil, was fastened to the bed beneath the buttocks of the subject for the collection of feces. The infants usually slept soundly on this bed, and

6. Levine, S. Z.; Wilson, J. R., and Kelly, M.: The Insensible Perspiration in Infancy and in Childhood: II. The Basal Insensible Perspiration of Infants, to be published.

7. Levine, S. Z., and Wilson, J. R.: The Respiratory Metabolism in Infancy and in Childhood: I. Basal Metabolism of Children, Am. J. Dis. Child. **31**:323 (March) 1926.

8. Yaglou, et al., in a series of articles in J. Am. Soc. Heat and Ventil. Engin., 1923 to 1925. Yaglou, C. P.: The Thermal Index of Atmospheric Conditions and Its Application to Sedentary and to Industrial Life, J. Indust. Hyg. **8**:11 (Jan.) 1926.

9. The insensible perspiration, as measured with the balance, includes gaseous emanations other than water vapor, notably carbon dioxide. The difference between the weight of the latter gas and the weight of the simultaneously absorbed oxygen constitutes from 5 to 15 per cent of the total loss of weight, or of the insensible perspiration, depending on the respiratory quotient.

observations were rarely interfered with by urinary or fecal losses. A similar bed, identically equipped, was invariably placed in close proximity to the one containing the subject during observations and served as a control. Changes in the weight of this bed afforded a measure of the interchange of moisture between it and the air of the room during an experiment, and corrections could be made therefore, if desired. Each bed with its contents, which included the clothes, several rubberized straps and safety pins for holding the subject in place and the basins for the urine and the stools, weighed approximately 1 Kg.

The clothes that the infants wore during basal observations were reduced to the minimum compatible with comfort, and consisted of a thin cotton undershirt, a nightgown of light weight flannel, cotton stockings and a specimen belt of unbleached muslin. They were varied only in experiments designed to study their influence on the insensible loss.

To ensure sleep during basal experiments, all the infants received small meals of modified cow's milk from one-half to two hours preceding observations. This procedure is also customary for ensuring sleep in measurements of the basal metabolism of infants. The food was weighed accurately to 10 mg., and the total weight was estimated as water in order to include the water resulting from the oxidation of the solid constituents within the body. This method of calculation was simpler than the one that included only the preformed water of the ingested food, and was entirely adequate for the purpose of the present study.

The apparatus is shown in the accompanying photograph.

EXPERIMENTAL PROCEDURE

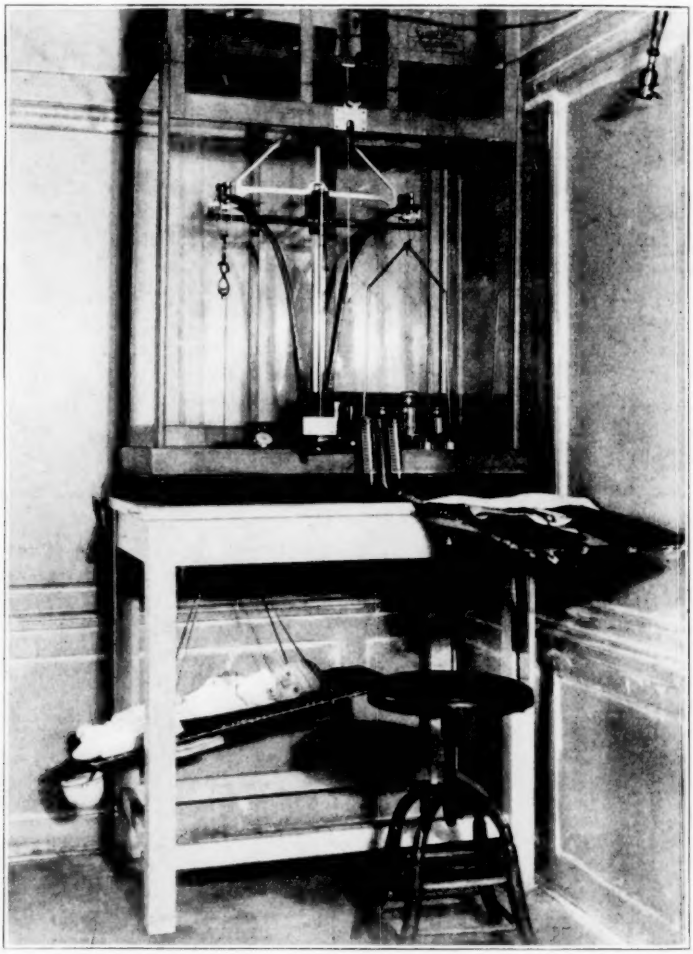
The bed used as a control and the experimental bed with the equipment previously enumerated were exposed to the air in the room throughout the night preceding the observations and were weighed early on the following morning. After the infant had voided, he was dressed and fed, and his rectal temperature was taken. The data were recorded. He was then placed on the bed, the basins for the urine and the stools, after being weighed, were adjusted, and the bed with the infant was suspended from the balance as shown in the photograph. As soon as the infant fell asleep, as it did usually from one-half to one hour following the meal, the initial weight was recorded. The difference between this weight and the weight of the bed and its contents yielded the weight of the subject at the beginning of the observation. Weighings were continued at intervals of approximately thirty minutes as long as the infant remained asleep (except in experiments designed to study the effect of activity). All observations therefore included two, and usually more, experimental periods and extended for from one to four hours. The reduction in weight, corrected for changes in the moisture content of the clothes and for urinary and fecal elimination, represented the insensible loss. At the end of the observation, the infant was undressed and removed from the frame, another specimen belt and tube were applied and the rectal temperature was again taken. The bed used as a control and the experimental bed were reweighed, and corrections for changes in their moisture content at the beginning and the end of the experiment were made whenever they were indicated. The subject remained under observation until he voided and this urine was added to that already collected during the experimental period.

The method described provides the necessary data for determining the water balance of infants over short periods, and for estimating the insensible perspiration and the urinary and fecal elimination per hour for the period of observation. Analyses of the ingested food and of the excreta for their water content were made when necessary for our purposes.

SOURCES OF ERROR

The method of weighings for estimating the insensible perspiration of infants is subject to a number of errors unless the technic is rigidly controlled.

The presence of different amounts of urine and feces in the bladder and the intestinal tract of a subject at the beginning and the end of an observation may



The balance and the experimental arrangements employed in the successive weighings of infants to determine the insensible perspiration under standard conditions.

introduce an appreciable error if these measurements are neglected.[10] This criticism does not hold for the present studies, since the excreta were accurately weighed whether they were or were not eliminated by the subject during the experimental period.

10. Nieman, A.: Der respiratorische Gaswechsel im Säuglingsalter, Ergebn. d. inn. Med. u. Kinderh. **11**:63, 1913.

Clothes necessarily introduce an error through an interchange of moisture between them, the subject and the atmosphere, until a condition of equilibrium is established. When a steady state has been reached, the moisture content of the clothes remains constant, provided the water vaporized by the subject and the relative humidity of the surrounding air does not change. The following precautions were taken in the present study to minimize the error arising from this source. Relatively few clothes and no bedding were used, measurements were postponed for at least one hour after the infant was clothed, and observations were invariably made during sleep and at a uniform atmospheric humidity. Experiments undertaken as controls, in which changes in the weight of the clothes were recorded at intervals of fifteen minutes following the dressing of the infants, showed that, generally, at the end of one hour further changes did not take place. For example, the clothes of an infant gained in weight 2.33 Gm. in the initial hour after dressing and only 0.38 Gm. in the following three hours. J. Meyer [2] found, in his work with infants, that an interval of fifteen minutes following the dressing was usually adequate for attaining an equilibrium of the moisture of the clothes. In view of these results, and in order to approximate the conditions existing in simultaneous measurements of the basal metabolism and of the water of vaporization as they are made in the respiration chamber, corrections for the minimal changes in the moisture content of the clothes were not made in the basal experiments. These measurements are, however, available in many instances and indicate that their exclusion does not materially change the basal figures. In the presence of visible perspiration, changes in the moisture content of the clothes may be considerable, and corrections for these changes were invariably made in the latter instances.

As previously mentioned, the insensible perspiration measured by the method of weighings includes carbon dioxide, as well as water vapor. The former gas, after the weight of the inhaled oxygen is deducted, comprises from 5 to 15 per cent of the total loss of weight, depending on the respiratory quotient.

The reported results are averages of at least two, and usually more, one-half hour experimental periods. The scatter of results for individual periods was appreciable at times (table 6), but deviations from the average values for entire observations rarely exceeded 10 per cent.

The uniform results obtained in repeated observations with the same infant on different days and under similar experimental conditions afford good evidence of the reliability of the method (table 7).

RESULTS

Nineteen normal and marasmic infants were studied in sixty-eight observations of from one to four hours' duration. They were afebrile and free from all evidence of acute disease throughout the experimental periods. Uniform conditions were maintained in all the experiments, except in those especially planned for studies of the effect of a particular environmental factor on the rate of the insensible loss. In the latter observations, a painstaking effort was made to vary only the agent under investigation and to maintain all other conditions constant. At least one observation as a control and one observation under the changed conditions were invariably made on the same infant. In addition, the same infant was frequently studied in repeated observations under the same

conditions in order to determine the constancy of the insensible perspiration on different days.

A systematic study of the following physiologic agents was made: (1) environmental temperature; (2) environmental humidity; (3) clothes; (4) activity; (5) food, including the fluid intake, and (6) the time interval between the last meal and the beginning of the observations. The majority of these agents were studied within a restricted range, since our main object in the present investigation was to ascertain the optimal environmental conditions for securing basal measurements. For this reason, observations have not yet been made of the effect of air in motion or of excessive caloric intake on the insensible loss. It is likely that some of the factors mentioned beyond the ranges studied, as well as other agents yet unrecognized, alter the rate of the insensible loss in infants. This assumption must, however, await experimental evidence for confirmation.

Environmental Temperature and Insensible Perspiration.—From two to six observations were made on each of eight infants under comparable conditions save that the room temperatures varied between the limits of 23 C. (74 F.) and 32 C. (90 F.) in the different experiments. For purposes of comparison, corrections for changes in the moisture content of the clothes were made in all but three of these observations (experiments 11, 42 and 44). As previously mentioned, the clothes absorbed considerable moisture from the subject during observations at the higher temperatures in the presence of visible perspiration. The results appear in table 1.

Table 1 shows that the surrounding temperature, within the comparatively narrow range studied, altered the rate of insensible loss only when it was sufficiently high to induce visible perspiration. When sweating appeared, the water loss notably increased, rising more than threefold above the basal level in some instances. The temperature that induced sweating varied markedly with the different infants. One infant (experiment 83) perspired profusely at the comparatively low temperature of 79 F. (26 C), whereas another infant (experiment 26) did not perspire visibly at the higher temperature of 83 F. (28 C.). Below the borderline of visible perspiration, the rate of the insensible perspiration of infants was little affected by changes in the environmental temperature. Studies have not as yet been made of the insensible loss of infants at temperatures below 23 C., but the likelihood is that it remains constant at these lower temperatures so long as muscular activity (shivering) does not supervene. J. Meyer [2] did not find a change in the rate of insensible loss of infants at temperatures between 18 and 23 C. His infants, however, wore heavier clothes and were awake during the observations.

The method proposed by Yaglou and his collaborators [8] for correlating atmospheric conditions with subjective sensations as well as with certain physiologic reactions, such as pulse rate, rectal temperature, basal metabolism and loss of weight, in adults was also employed in the present study of the insensible perspiration of infants. By combining the wet and dry bulb temperatures, Yaglou constructed a scale of so-called effective temperatures and established a comfort zone for adults that was conducive to the optimal physiologic reactions. This comfort zone

TABLE 1.—*Effect of Environmental Temperature on Insensible Perspiration*

Subject	Experiment	Duration of Observation, Minutes	Temperature Average, F.			Insensible Perspiration, Gm. per Hour	Visible Perspiration
			Dry Bulb	Wet Bulb	Effective*		
M. K.	17	136	79	72	75	5.71	Absent
	11†	72	81	66	74	5.50	Absent
	21	123	84	71	77	15.58	Present
	23	131	84	71	77	15.85	Present
	25	65	85	75	79	15.74	Present
	14	142	86	73	79	17.18	Present
O. H.	6	105	79	63	72	5.66	Absent
	16	125	79	68	74	5.94	Absent
	20	120	87	73	79	15.49	Present
	13	100	90	77	82	19.25	Present
A. E.	18	57	80	67	74	6.03	Absent
	26	115	83	71	77	6.37	Absent
	15	122	84	71	77	9.95	Present
	24	114	86	68	77	15.94	Present
	22	106	86	74	79	17.36	Present
M. V.	34	102	78	63	72	5.63	Absent
	35	98	83	65	75	12.99	Present
W. B.	44†	182	76	56	68	8.76	Absent
		78	76	56	68	9.26	Absent
	42†	241	79	60	71	11.94	Present
E. K.	37	155	78	67	71	7.83	Absent
	40	149	74	55	67	8.15	Absent
	39	128	80	65	73	15.14	Present
R. M.	82	79	75	63	70	7.05	Absent
	81	141	80	62	72	13.93	Present
	80	114	84	74	79	23.24	Present
T. S.	85	136	76	56	68	8.49	Absent
	84	97	80	67	74	12.82	Present
	83	112	79	70	75	13.66	Present

* The effective temperature was estimated from the standard chart of Yaglou (footnote 8).
† Corrections for changes in the moisture content of the clothes were not made in these experiments.

for the adults studied ranged between 63 and 71 F. on the scale of effective temperatures. The zone of effective temperatures within which the insensible perspiration of the present group of infants maintained the basal rate was, in general, slightly higher than the comfort zone established for adults, reaching the high level of 77 F. in one instance (experiment 26) and averaging 69 F. for all of the basal observations to be reported later.[6] The fact that the infants were studied during sleep and the adults while awake may partially explain the discrepancy.

In passing, it seemed of interest to consider the profound influence of high temperatures on the rate of the loss of water in relation to clinical observations that infants are greatly benefited by an increased fluid intake during the summer months. If the values obtained in these

observations of from one to two hours are expanded to twenty-four hours, it is seen that the water vaporized daily through the skin and lungs of infants from 2 to 5 months old (weighing from 3 to 5 Kg.) frequently rose from the minimal values of approximately 150 Gm. to the extraordinarily high level of 500 Gm. This estimated daily increase of 350 Gm. is conservative, since it covers the loss in weight only under basal conditions and does not include the dissipation of water during periods of wakefulness and periods of especially vigorous crying. In the latter periods, the loss may be assumed to be disproportionately high in the presence of sweating. The data afford experimental evidence of the desirability of increasing markedly the customary fluid intake during hot weather, especially since there is evidence at hand, to be published later, which suggests that the augmented rate of the loss of water through the skin and the lungs during sweating is not entirely compensated for by a diminution in the urinary output.

Environmental Humidity and Insensible Perspiration.—Most workers [11] have agreed that the relative humidity of the surrounding air exerts only a trivial influence on the insensible loss under ordinary conditions. The present data include from two to three observations on each of four infants under uniform conditions save for the relative humidity of the surrounding air, which ranged between 26 and 73 per cent. The absence of special methods for regulating the moisture content of the air of the room made it impossible to study the insensible perspiration outside of the range mentioned.

Within the range studied, the values for insensible perspiration were not noticeably affected by alterations in the relative humidity. Maximal deviations for repeated observations on the same infant did not exceed 5 per cent, except in experiment 59, of twenty-one minutes' duration, in which the average deviation was 8 per cent. Until further data are available, one cannot be certain that the insensible loss of infants is maintained at a constant and basal level outside these limits of relative humidity, especially since previous studies by Rubner with the calorimeter [12] showed twofold and threefold increases in the vaporization of water of dogs and guinea-pigs, with a fall in the relative humidity from 69 to 31 per cent.

Clothes and Insensible Perspiration.—A number of preliminary experiments were made with various materials, including wool, linen,

11. Eimer, K.: Untersuchungen über das Wesen der Perspiration, Arch. f. exper. Path. u. Pharmakol. **125**:150, 1927. Camerer: Der Stoffwechsel des Kindes, Tübingen, 1896. Hecht, A. F.: Zur Kenntnis der extrarenalen, insbesondere pulmonalen Wasserausscheidung, Ztschr. f. Kinderh. **38**:193, 1924. Footnote 2.

12. Rubner, M.: Die Beziehung der atmosphärschen Feuchtigkeit zur Wasserdampfabgabe, Arch. f. Hyg. **11**:137, 243 and 255, 1890.

flannel and cotton, before a final decision was made on the standard clothes for basal observations. It is unnecessary to consider the detailed data, but, in general, the results indicated that the different materials did not consistently alter the rate of insensible loss, provided they were not sufficiently heavy to induce sweating and provided the time interval between dressing and the onset of the experimental period was adequate to establish a state of equilibrium between the cutaneous loss of water on the part of the infant and the moisture content of the clothes and the atmosphere. The results of two groups of comparable observations on three infants are presented in table 3. In these experiments, at least one hour elapsed between the dressing of the infants and the beginning of the basal periods. The only variable factor in these experiments was the clothing.

TABLE 2.—*Effect of Relative Humidity on Insensible Perspiration*

Subject	Experiment	Duration of Observation, Minutes	Relative Humidity, Average per Cent	Insensible Perspiration, Gm. per Hour
M. K.	2	76	26	7.89
	1	216	40	7.78
O. H.	9	176	30	5.05
	7	72	41	5.04
	8	111	54	5.09
M. K.	11	72	33	5.50
	17	99	73	5.48
E. K.	40	149	27	8.15
	37	155	40	7.83
E. W.	60	76	35	4.74
	61	76	37	4.58
	59	21	47	4.10

The insensible loss of water by one infant (O. H.) diminished slightly and that of the other two infants (M. K. and M. V.) increased markedly in the observations with the heavier clothes. Although perspiration was not perceptible, the clothes felt moist to the touch at the end of the latter experiments. Unfortunately, corrections for changes in their moisture content were not made in the early experiments with the first two infants. Had they been made, the differences might have been even more marked.

It was not considered necessary for our purposes or advisable to make studies on infants devoid of all clothes or swathed in excessively heavy clothes, since the primary object was to ascertain the optimal conditions for making basal measurements. Previous work has shown that the insensible perspiration of infants remains essentially the same whether they are naked or lightly clothed.[2] The standard clothes finally adopted in basal observations at room temperatures between 23 and 27 C. consisted of a thin cotton undershirt, cotton stockings, a nightgown of outing flannel and a specimen belt of unbleached muslin.

Muscular Activity (Crying) and Insensible Perspiration.—One might infer from the close relation existing in infants between the production of heat and the loss of heat by way of vaporization of water through the skin and lungs [5] that muscular activity, which exerts such a notable influence on the respiratory exchange, would also augment the insensible perspiration even in the absence of visible perspiration. A method is not at present available for grading quantitatively the intensity of muscular activity in infants. This obviously must vary with the vigor of crying, the degree of restlessness and other immeasureable factors. As an approximate measure of activity, observations were apportioned into sleeping and wakeful periods, and the proportion of the latter periods occupied by feeding, quiet, restlessness and crying were noted. The data comprise thirty-seven periods of observation on seven infants

TABLE 3.—*Effect of Clothes on Insensible Perspiration*

Subject	Experiment	Duration of Observation, Minutes	Insensible Perspiration, Gm. per Hour	Clothes*
M. K.	11	72	5.50	A
	17	136	5.65	A
	1†	98	7.78	B
	2†	76	7.89	B
	3	197	6.77	B
O. H.	16	125	5.76	A
	5	123	5.37	A
	7	72	5.04	B
	8	111	5.09	B
	9	116	5.05	B
M. V.	29	73	7.39	A
	28†	113	10.31	C

* A, standard clothes, consisting of thin cotton shirt, nightgown of outing flannel, specimen belt of unbleached muslin and cotton stockings; B, heavier clothes, comprising the standard apparel together with a canvas mattress cover, linen sheeting, three towels of bird's-eye linen and several pads of nonabsorbent cotton; C, a woolen sweater, a cap and booties, in addition to the standard apparel.

† The clothes felt moist to the touch at the end of these experiments.

under comparable conditions save for various states of activity. The results appear in table 4.

In these observations, the infants remained awake for from 17 to 100 per cent of the entire experimental period, and their insensible loss rose from 11 to 196 per cent above the respective basal levels obtained during sleep. They rose proportionately less in the periods when the infants were awake but quiet than in the periods of crying, but they remained of sufficient magnitude to exclude them from the basal results. A rough parallelism was evident between the intensity and the duration of crying and the percentage rise above the basal insensible loss, but it was far less consistent than the correlation found by Murlin and his associates [13] between the rise in the production of heat of new-born infants and the duration of crying.

13. Murlin, J. R.; Conklin, R. E., and Marsh, M. E.: Energy Metabolism of Normal, New-Born Babies, with Special Reference to Influence of Food and Crying, Am. J. Dis. Child. **29**:1 (Jan.) 1925.

Fluid Intake and Insensible Perspiration.—The present data are limited to studies of the effect of moderate variations in the fluid content of single meals on the insensible perspiration during comparatively short periods following these meals. An attempt was not made to study the extreme conditions of thirst and of excessive ingestion of fluid over prolonged periods. From two to four observations were made on each of six infants under comparable conditions and following the same meal,

TABLE 4.—*Effect of Activity on Insensible Perspiration*

Subject	Experiment	Duration of Observation, Minutes	Insensible Perspiration, Gm. per Hour	Activity
M. K.	11	72	5.50	Asleep
	12	78	8.76	Awake, coughing intermittently 77% of period
M. L.	36	32	11.81	Asleep
	52	52	13.15	Awake, moderately quiet 58% of period
J. N.	45	75	14.82	Asleep
	44	44	19.31	Awake, quiet throughout
R. F.	50	45	6.78	Asleep
	80	80	9.04	Awake, restless 50% of period
K. F.	54	35	8.57	Asleep
	122	122	9.84	Awake, restless 17% of period
F. W.	59	21	4.10	Asleep
	99	99	7.64	Awake, moderately quiet throughout
	61	76	4.46	Asleep
	23	23	5.74	Awake, very quiet throughout
	62	109	4.95	Asleep
	40	40	7.41	Awake, quiet 68% of period
	63	19	4.74	Asleep
	197	197	9.28	Fed; awake, quiet 71% of period
	66	109	4.51	Asleep
	88	88	11.43	Awake 95% of period; crying 72% of period
	67	89	7.08	Asleep
	110	110	10.91	Awake, moderately quiet 65% of period
	68	155	4.34	Asleep
	57	57	12.85	Fed; awake 78% of period; crying 49% of period
	69	223	5.11	Asleep
	50	50	13.13	Fed; awake, moderately quiet 62% of period
	70	201	5.39	Asleep
	47	47	15.11	Fed; awake 70% of period; crying 45% of period
R. H.	73	174	8.13	Asleep
	83	83	11.29	Fed; awake, quiet 85% of period
	74	145	7.74	Asleep
	110	110	14.45	Fed; awake, moderately quiet throughout
	75	147	6.82	Asleep
	113	113	12.46	Fed; awake, moderately quiet throughout
	76	160	5.51	Asleep
	120	120	14.85	Fed; awake 90% of period; crying 33% of period

without and with the addition of varying amounts of water. The added water only occasionally exceeded 100 Gm. and usually did not suffice to raise the fluid content more than two-fold above that of the control meal. The total weight of the meals, with one exception (experiment 42), ranged between 72 and 207 Gm. and between 18 and 52 Gm. per kilogram of body weight. The results appear in table 5.

It is evident from table 5 that the insensible perspiration maintained a uniform rate despite the minor fluctuations in the fluid content of the preceding meals. Maximal deviations under the different conditions of

fluid intake exceeded 8 per cent only in experiments 42 and 67. In these observations, the fluid intake was increased from 174 to 530 Gm. and from 75 to 185 Gm., respectively, and the loss in weight rose from 8.76 to 10.68 Gm. per hour and from 4.74 to 7.08 Gm. per hour. The infants perspired visibly during both the latter observations. It is possible that, under certain conditions, excessive ingestion of fluid may induce sweating and thus augment the loss of weight.

The uniform results in the remaining observations, in which visible perspiration was absent, afforded good evidence that the previous administration of small meals did not appreciably modify the basal insensible loss, provided an adequate interval was allowed to elapse between the ingestion of the meal and the onset of the observation (table 6). The

TABLE 5.—*Effect of Fluid Intake on Insensible Perspiration*

Subject	Experiment	Duration of Observation, Minutes	Fluid Intake, Gm.	Insensible Perspiration, Gm. per Hour
O. H.	5	123	120	5.37
	6	105	167	5.66
	5	121	200	5.21
A. E.	18	106	141	6.03
	26	115	182	6.37
W. C.	30	94	81	5.07
	33	33	116	5.45
W. B.	44	182	174	8.76
	42*	121	530	10.68
E. W.	62	109	72	4.95
	63	19	75	4.74
	67*	89	185	7.08
	69	223	182	5.11
R. H.	73	83	119	8.13
	74	145	207	7.74

* Visible perspiration was present at the time of these observations, although the effective temperatures were only 71 and 74 F., respectively.

standard meals that were finally adopted for basal measurements of the insensible perspiration of infants under 1 year of age consisted usually of dilutions of modified cow's milk, low in calories (rarely exceeding 25 calories per kilogram of body weight), of fluid consistency and weighing between 20 and 40 Gm. per kilogram of body weight. Similar meals are universally employed when measurements are made of the basal metabolism of infants. Meals weighing less than 20 Gm. per kilogram were not studied, since these minimal meals are not conducive to sound sleep and were, therefore, not considered as satisfactory as the slightly larger meals for basal estimations.

This conclusion is in accord with that of most workers,[14] who found that an increase in the fluid content of a single meal leads to an augmented output of urine without altering appreciably the extrarenal

14. Footnote 11. Laschtschenko: Ueber den Einfluss des Wassertrinken aug Wasserdampf-und CO_2-abgabe des Menschen, Arch. f. Hyg. **30**:145, 1898.

loss of water. De Rudder,[2] however, expressed the belief that the insensible perspiration is entirely dependent on the water intake. His observations in which alterations in fluid intake persisted for several days are not comparable with the present series.

The Time Interval Following the Last Meal and Insensible Perspiration.—A consideration of the degree and the persistence of the stimulating effect of the previous meal on the insensible loss was pre-

TABLE 6.—*Effect of Duration of Interval Following Feeding on Insensible Perspiration*

Subject	Experiment	Start to End of Observation, Minutes Following Feeding	Number of Periods	Insensible Perspiration, Gm. per Hour	
				For Individual Periods	Average
M. K.	3	11 to 101	3	7.73; 8.26; 7.34	7.76
		101 to 237	5	6.68; 6.63; 6.00; 5.33; 5.79	6.12
	17	33 to 71	1	6.08	6.08
		71 to 168	3	5.78; 5.09; 5.71	5.48
O. H.	5	39 to 69	1	6.00	6.00
		69 to 161	4	5.33; 5.46; 5.22; 4.71	5.16
	6	38 to 80	2	7.10; 7.42	7.32
		80 to 147	3	6.00; 6.52; 6.49	6.32
A. E.	26	28 to 86	2	6.18; 6.32	6.25
		86 to 140	2	7.20; 7.64	7.42
M. V.	29	37 to 66	1	7.66	7.66
		66 to 111	2	6.79; 6.67	6.74
	34	40 to 72	1	5.29	5.29
		72 to 143	2	5.63; 5.56	5.59
E. K.	37	47 to 70	1	8.00	8.00
		146 to 214	3	6.92; 6.37; 6.15	6.47
	40	40 to 59	1	9.60	9.60
		59 to 189	4	7.42; 7.58; 7.83; 6.78	7.40
K. R.	47	46 to 110	1	9.45	9.45
		110 to 165	2	8.00; 7.06	7.53
J. S.	57	30 to 78	1	5.60	5.60
		78 to 146	2	5.40; 5.14	5.33
E. B.	58	37 to 59	1	19.09	19.09
		72 to 134	3	13.33; 13.33; 12.00	12.89
E. W.	66	31 to 60	1	4.55	4.55
		60 to 140	3	4.44; 4.44; 4.62	4.50
	68	33 to 64	1	4.71	4.71
		64 to 191	4	4.85; 4.14; 4.00; 3.89	4.25
	69	26 to 52	1	7.06	7.06
		52 to 249	5	5.63; 4.68; 5.45; 4.69; 4.12	4.86
	70	32 to 61	1	8.27	8.27
		61 to 233	5	5.14; 4.55; 4.41; 5.24; 5.00	4.90

requisite for achieving reliable measurements of the basal insensible perspiration of infants. Table 6 presents the results of sixteen observations on nine infants in which weighings began during the initial hour following feeding and in which they continued for the subsequent period of from two to three hours. The individual (column 5) and the average (column 6) results for both periods are placed directly beneath each other for comparison.

It is obvious that a striking discrepancy exists between the figures for the initial hour following the meal and those for the subsequent period of from two to three hours. The values, except in experiments

26 and 34, were notably higher in the former than in the latter periods. These results, which are in accord with previous work,[15] indicate the necessity of delaying basal measurements of the insensible perspiration of infants for at least one hour after the ingestion of food. For a similar reason, measurements of the basal metabolism of infants are commonly delayed for an equivalent period following feeding in order to minimize any specific dynamic effect that may be present as a result of the food previously ingested.

The extent of the scatter of the results for individual periods of an experiment furnishes a good index of the reliability of the method. Column 5 of table 6 shows that the figures for the individual half-hour periods continued to exhibit trivial fluctuations even after an essentially uniform and basal rate was established. The scatter, however, was negligible, maximal deviations from the average figure for the entire observation exceeding 10 per cent in only two of the sixteen experiments (nos. 3 and 68) and 15 per cent in only one instance (no. 69). The comparatively slight scatter for the individual periods of these experiments compares favorably with the scatter frequently present in duplicate measurements of the respiratory exchange of infants. The presence, however, of even slight variations, whether they arise from technical errors or from intrinsic fluctuations in the insensible loss of subjects from minute to minute, made it highly desirable to include in the reported results only the average figures of at least two and preferably more periods.

The Constancy of the Insensible Perspiration of Infants.—The data presented in the preceding sections of this paper are adequate to establish a circumscribed range of environmental conditions within which fluctuations of any of the factors did not apparently modify the rate of insensible loss in infants. A knowledge of these standard conditions made it possible to investigate the intrinsic constancy of this measurement from day to day as obtained by the method of weighings. Repeated observations were made on nine infants on different days under experimental conditions that were essentially uniform or that fell within the range previously shown to be without effect on the insensible loss. The results appear in table 7.

The insensible perspiration of all the infants maintained a constant rate on the different days under the accepted standard condition. Variations were trivial, maximal deviations in single observations never exceeding 8 per cent from the average value for the whole group, and being 5 per cent or less in all but three of the twenty-nine observations (experiments 6, 37 and 69). Besides establishing the constancy of the

15. Footnote 2. Pahnke, H.: Ueber den Wasserhaushalt des fiebernden Säuglins, Ztschr. f. Kinderh. **44**:494 (Nov.) 1927.

insensible loss of water by infants, these uniform results place the experimental error of the method at less than 10 per cent. This error is well within that generally accepted as adequate for biologic measurements.

COMMENT

The conflicting evidence previously reported in the literature regarding the constancy of the insensible perspiration of infants suggested the present group of studies. The results demonstrate that normal and marasmic infants maintain a basal rate of insensible perspiration under

TABLE 7.—*Control Observations Showing Constancy of Insensible Perspiration Under Standard Conditions*

Subject	Date	Experiment	Insensible Perspiration, Gm. per Hour	
			Total	Per Kg.
M. K.	6/ 1/27	1	7.78	1.93
	6/ 2/27	2	7.89	1.92
	6/ 6/27	4	8.13	1.94
O. H.	6/ 7/27	5	5.37	1.41
			5.21	1.36
	6/ 8/27	6	5.66	1.44
	6/ 9/27	7	5.04	1.35
	6/10/27	8	5.09	1.39
	6/13/27	9	5.05	1.33
A. E.	7/25/27	18	6.03	1.21
	8/ 2/27	26	6.37	1.25
W. C.	12/ 2/27	30	5.07	1.38
	12/ 9/27	33	5.45	1.43
H. G.	12/ 2/27	31	5.86	1.16
	12/ 5/27	32	5.33	1.05
E. K.	12/28/27	37	6.79	0.87
	12/29/27	38	7.50	0.97
	1/ 4/28	40	7.68	0.98
W. B.	2/ 6/28	44	8.76	1.32
			9.26	1.40
K. F.	4/13/28	53	8.35	1.40
	4/17/28	54	8.57	1.45
E. W.	5/30/28	60	4.74	1.23
	5/31/28	61	4.58	1.19
	6/ 1/28	62	4.95	1.26
	6/ 4/28	63	4.74	1.21
	6/ 7/28	66	4.51	1.14
	6/ 9/28	68	4.34	1.09
	6/11/28	69	5.11	1.29

well defined environmental conditions, and that this rate remains essentially constant from day to day. The conditions that were finally accepted as yielding basal measurements comprised environmental temperatures between 23 and 25 C., with the minimal amount of clothing compatible with comfort, relative humidities between 25 and 50 per cent and the ingestion of small meals at least one hour preceding observations, which were invariably made during sleep. It is not claimed that these standard conditions necessarily yielded absolutely minimal values for this measurement, but they seemed the most applicable for general use, and they have the added advantage of paralleling closely the standard conditions commonly adopted in measuring the basal metabolism of infants.

The demonstration of the constancy of the basal rate of insensible perspiration in infants as measured by the method of weighings is of physiologic and clinical interest. It makes possible the construction of standard tables for this measurement analogous to the standards at present available for basal metabolism. In addition, it opens up a comparatively neglected field of investigation, namely, that of the water exchange in certain infantile conditions associated with a probable derangement of water metabolism (hydrolability, dehydration, edema). Such studies are now in progress and will be reported later.

SUMMARY AND CONCLUSIONS

Differences in environmental conditions, as they affect the insensible perspiration, were studied in sixty-eight observations of from one to four hours' duration on nineteen normal and marasmic infants by the method of weighings. When the technic, which has been fully described, is carefully controlled, the experimental error of the method is probably less than 10 per cent.

The following standard conditions were adopted for securing basal measurements: (1) a range of environmental temperature between 23 and 25 C. in the absence of visible perspiration; (2) an environmental relative humidity between 25 and 54 per cent; (3) the minimal amount of clothing compatible with comfort, that is, a thin cotton shirt, a nightgown of light weight flannel, cotton stockings and a rubber mattress without bedding; (4) a condition of sleep and the absence of muscular activity, and (5) the ingestion, at least one hour preceding the onset of observation, of small meals containing fewer than 25 calories per kilogram of body weight and weighing between 20 and 40 Gm. per kilogram. It is not claimed that these standard conditions necessarily yielded absolutely minimal values, but they seemed most applicable for general use.

The stimulating effect on the rate of insensible loss induced by sweating, muscular activity and food intake in the initial hour following ingestion was observed.

The basal rate of insensible perspiration in infants under the standard conditions mentioned was found to be constant from day to day, maximal deviations in repeated observations on different days rarely exceeding 10 per cent.

The results afford good evidence of the reliability of the method of weighings and demonstrate the constancy of the basal rate of the insensible perspiration of infants under standard environmental conditions. The clinical and physiologic importance of these results has been briefly discussed.

Case Reports

LATE DEATH AS A RESULT OF CEREBRAL HEMORRHAGE AT BIRTH *

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The late results of cerebral hemorrhage at birth are well known to clinicians in general since the classic studies of Little [1] and McNutt.[2] The obstetrician and the pediatrician especially are familiar with the frequent incidence of cerebral hemorrhage at birth and the numerous deaths which occur during the first few days of life as a result. In a recent report, Green [3] stated that intracranial hemorrhage is the most frequent cause of death in the new-born infant. He found this lesion in fifty-five of 177 consecutive necropsies (31 per cent of cases) performed at the Boston Lying-In Hospital. Green's report is a fair example of the experience in most large clinics.

As a rule, when death follows cerebral hemorrhage at birth, it is within the first three or four days. In a series of fifty cases observed by Ford,[4] in which the condition had been diagnosed as cerebral hemorrhage, only seven survived for two weeks. If an infant with a cerebral hemorrhage survives the first few days, the prognosis in regard to life is good. It is known also that many cases of cerebral hemorrhage at birth occur in which there are no symptoms other than possible changes in the cerebrospinal fluid, depending on the location of the hemorrhage, and in which the infant may make an uneventful recovery in every respect.

The case to be reported does not belong in any of the classifications mentioned. If one were to seek a classification for this case, it might be put under such a heading as "prolonged lucid interval following cere-

* Submitted for publication, Aug. 20, 1928.

* From the Leon Klein Fund of the Michael Reese Hospital, the Sarah Morris Hospital for Children, and the Nelson Morris Institute for Medical Research.

1. Little, W. J.: On the Influence of Abnormal Parturition, Difficult Labors, Premature Birth, Asphyxia Neonatorum, on the Mental and Physical Conditions of the Child, Especially in Relation to Deformities, Tr. Obst. Soc., London **3**: 293, 1862.

2. McNutt, S. J.: Double Infantile Spastic Hemiplegia with the Report of a Case, Am. J. M. Sc. **89**:58, 1885.

3. Green, T. C.: Intracranial Hemorrhage in the Newly-Born, Boston M. & S. J. **197**:1302 (Jan. 12) 1927.

4. Ford, F. R.: Cerebral Birth Injuries and Their Results, Medicine **5**:121 (Aug.) 1926.

bral hemorrhage at birth" or "late death as a result of cerebral hemorrhage at birth."

In the case reported, death occurred at the age of 1 month as a result of a cerebral hemorrhage which took place at the time of birth. Such late deaths from cerebral hemorrhage at birth are rare, and I have been able to find a record of only one other at all similar.

REPORT OF A CASE

History.—The mother of the child was a white woman, aged 22 years. Two and one-half years previous to the birth of this child she had aborted spontaneously during the third month of pregnancy, following which a curettage was performed. A year later she aborted again, also during the third month of pregnancy. Fibroids were suspected, and an exploratory laparotomy disclosed a bicornate uterus containing multiple fibroids. The right horn was amputated and the uterus found to contain decidual tissue. The postoperative course was uneventful. Eighteen months later, on Jan. 1, 1927, she entered the maternity ward of Michael Reese Hospital at the end of the ninth month of pregnancy. She had experienced labor pains, and the bag of waters had ruptured one hour previous to admission. After a prolonged dry labor of twenty-six hours, a male infant weighing 3,520 Gm. (7 pounds, 11 ounces) was delivered in the right occipito-anterior position following an episiotomy. Forceps were not applied. The child was somewhat cyanotic at birth but recovered in a few hours, and up to the time of his terminal illness was apparently normal.

On the morning of January 31, the mother noticed that the child was slightly blue and that his skin felt cool to her touch. Otherwise he seemed well, except for some loss of appetite. A physician was called and warm baths and hospitalization were advised. During the day cyanosis appeared and disappeared at intervals. Another physician, who examined the child in an interval between cyanotic attacks, told the mother that he was well and did not require medical attention.

The next morning the cyanotic attacks occurred at more frequent intervals and with greater severity. The child seemed unable to nurse and coughed occasionally. The stools which had been yellow and soft became foul-smelling and green, and finally scanty and black, apparently starvation stools. The mother then brought the child to the Sarah Morris Hospital Dispensary, where I saw him for the first time.

Examination.—The child was in the midst of a severe cyanotic attack; the expression was listless and he appeared moribund. The weight was 3,721 Gm. (8 pounds, 3 ounces); the temperature was 98.6 F., rectally. The anterior fontanel measured 3 by 4 cm., was flat and not under tension. There was no evidence of injury to the scalp, skull bones or spine. Both pupils were small but not pinpoint and reacted to light. Both ear drums were red, and the right drum seemed bulging. On paracentesis, pus was not obtained. Occasionally, when the child assumed a position of opisthotonos, rigidity of the neck occurred. The respirations were slow, 12 per minute, and irregular during the cyanotic attacks; they were normal in the intervals. The cardiac area was not enlarged to percussion. During the cyanotic attacks the heart rate became slow, 60 per minute, occasionally irregular, and the tones extremely weak. There were no murmurs at any time. In the intervals between the attacks the heart rate, rhythm and tones were normal.

There seemed to be a slight impairment of resonance over the left pulmonary apex anteriorly and over both apexes posteriorly, with harsh breathing in these

areas, but no râles or bronchial breathing. The liver and spleen were palpable but did not seem enlarged. The knee reflexes were brisk. The Brudzinski, Babinski and Kernig signs were negative. During the intervals between the cyanotic attacks, which occurred with irregular frequency, sometimes every minute, sometimes not oftener than every two hours, the child seemed perfectly well.

The infant was admitted to the service of Dr. A. Levinson. (He gave the permission to report this case.) On admission the impression was that the patient had acute bilateral otitis media and early bronchopneumonia. In arriving at a diagnosis, the following conditions had to be considered: (1) foreign body in the upper respiratory passages, (2) morphine poisoning, (3) congenital heart disease, (4) atelectasis or massive collapse of the lungs, (5) enlarged thymus, (6) encephalitis or meningitis and (7) cerebral hemorrhage.

Immediately after admission a fluoroscopy was performed, and roentgen-ray films were taken of the chest. There was no roentgenographic evidence of a foreign body in the upper respiratory passages or a pathologic condition of the lungs. The heart shadow appeared normal, and there was no suggestion of mediastinal enlargement. The blood counts and the urine were normal.

During the remainder of the day of admission and that night the child seemed comfortable and nursed fairly well. The breasts of the mother were pumped, and the child was given a bottle containing 2 ounces of breast milk every two hours.

The following morning the temperature was 98.8 F. The apathy and cyanotic attacks continued. The anterior fontanel was depressed. The pupils were pinpoint. The right external auditory canal drained bloody fluid. Between the cyanotic attacks the pulse rate was 160; the tones were loud and apparently of good quality. There were numerous moist râles throughout both lungs. The throat appeared acutely red. Palpation of the pharynx for a retropharyngeal abscess was negative. At times the jaws were so spastic that the mouth could not be opened. The Brudzinski and Kernig signs were negative. The Babinski and Oppenheim reflexes were present and exaggerated. Occasionally, the lower extremities were rigid. A satisfactory examination of the eyegrounds could not be made. The results of the von Pirquet test were negative.

Lumbar puncture yielded a water-clear, colorless fluid, apparently under normal pressure. The results of the Ross-Jones, Pandy and benzidine tests were negative. The cell count was 3 polymorphonuclear leukocytes and 2 red blood cells per cubic millimeter. The normal fluid practically ruled out encephalitis or meningitis, but the possibility that the child was suffering from a cerebral hemorrhage remained.

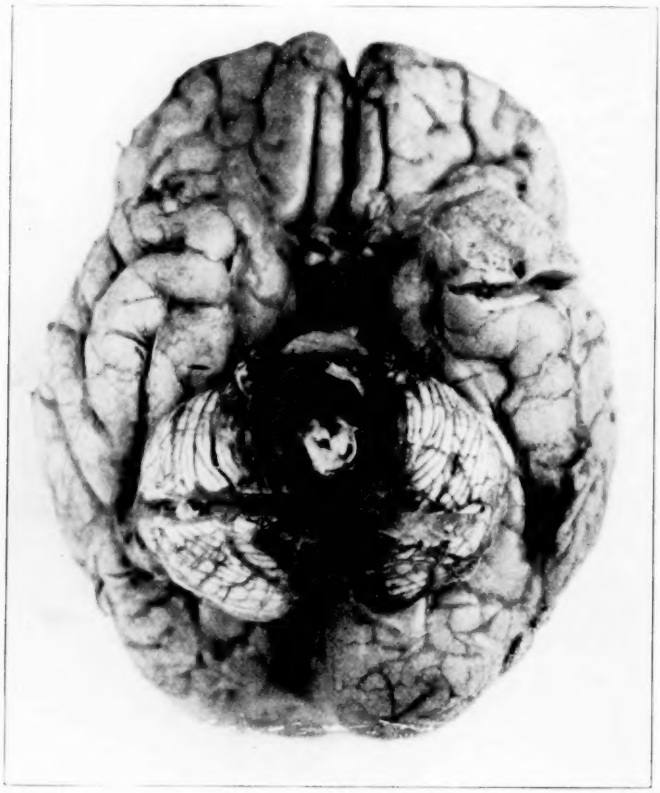
On the evening of the second day of admission the temperature rose to 102.8 F. The cyanotic attacks became more frequent and the respirations more labored and irregular. At times, Cheyne-Stokes respirations were observed. Tremors and stiffening of the body occurred at frequent intervals. The child failed to respond to stimulation, and died on the afternoon of the third day after admission, at the age of 34 days.

The final diagnosis recorded on the chart before the body was sent to the morgue for necropsy was: cerebral hemorrhage involving the medulla oblongata, acute bilateral otitis media and terminal bronchopneumonia.

Necropsy Report.—The necropsy was performed by Dr. Benson Bloom, resident pathologist, within one-half hour after death. The thymus weighed 6 Gm. and appeared grossly normal. Both lungs were edematous and contained small scattered areas of congenital atelectasis, but not in excess of that frequently found in infants of this age. There were also small scattered areas of bronchopneumonia throughout both lungs. The heart weighed 28 Gm. and was grossly normal. The

suprarenals weighed 3 Gm. each and were grossly and microscopically normal; nothing pathologic was discovered in the other abdominal organs.

As cerebral hemorrhage was suspected, the calvarium was opened with extreme care. There was no evidence of injury to any of the skull bones. Above the tentorium, the brain appeared normal. At the base of the brain, however, there was a firm clot beneath the leptomeninges in which organization by connective tissue was taking place. This hemorrhage involved the region of the optic chiasm and extended backward, filling the interpeduncular region, continuing over the pons and medulla oblongata and spreading laterally for a short distance over the



Slightly less than natural size of the brain after fixation in formaldehyde. The transverse sections through the pons and the cerebellum illustrate the thickness of the clot in these regions.

lower surface of the cerebellum on both sides. The hemorrhage completely surrounded the neuraxis at the point of junction of the spinal cord and medulla oblongata, apparently obliterating the region of the cisterna magna, continued dorsally over the vermis, where the hemorrhage was thickest (about 1 cm.), and thinned out toward the upper surface of the cerebellum, as shown in the accompanying illustration. That an internal hydrocephalus did not result is probably due to the fact that the lateral foramina were unobstructed by the clot. Over the medulla oblongata, the clot was about 3 mm. thick. For the most part, the area

of the hemorrhage was bluish black. Microscopic examination showed an old, organizing blood clot. As a result of the necropsy, it seemed probable that death was secondary to cerebral hemorrhage which, from the appearance of the clot, occurred presumably at birth. Other corroborative evidence regarding the age of the hemorrhage lay in the fact that clear, colorless cerebrospinal fluid was obtained the day before death.

From a fairly large experience with premature infants,[5] in whom cerebral hemorrhage occurs with great frequency, it has been learned that hemorrhages, when not interstitial or epidural, produce xanthochromia of the cerebrospinal fluid which lasts for several weeks before the fluid becomes colorless. Red blood cells are seldom found in the fluid from ten to fifteen days after the occurrence of even a very large hemorrhage. The clinical course of the child's terminal illness may be explained on this basis.

After a prolonged labor in a primiparous woman, with a uterus previously disposed to pathologic labor as a result of two abortions and a plastic operation for a congenital anomaly, a child was born who did not show any signs of injury at birth except a transient cyanosis. In view of subsequent developments, this was probably due to cerebral hemorrhage, but this cannot be positively stated since transient cyanosis occurs in the new-born infant even when cerebral hemorrhage is not present. The cerebral hemorrhage which occurred at birth was subpial, the kind of hemorrhage which occurs typically in premature infants but not so commonly in full-term infants. The hemorrhage may have had one or several origins, and as it spread, the pia was dissected away from the brain substance. Had the pia not yielded to the dissecting action of the oozing blood, the hemorrhage might have been checked, and no ill results followed; or, if the hemorrhage had continued, death would have resulted shortly after birth from pressure on the brain stem. As it was, the child survived until the age of 1 month, at which time contraction of the clot in the process of organization gave rise to embarrassment of the medullary centers, particularly that of respiration, with resulting cyanosis, and ultimately respiratory paralysis and death.

COMMENT

The case presented is of the greatest interest, not only because of the rarity of the lesion, but also from the standpoint of differential diagnosis. The single, prominent symptom that any one diagnosis would have to explain was the intermittent or paroxysmal cyanosis. Had the infant just been delivered or if he were only a few days old, a diagnosis of subtentorial cerebral hemorrhage would have been obvious, but, on

5. Glaser, Jerome: The Cerebrospinal Fluid of Premature Infants, Am. J. Dis. Child. **36**:195 (Aug.) 1928.

account of the infrequency of the appearance of acute symptoms of cerebral hemorrhage without obvious cause in a child 1 month of age, it was thought necessary to rule out the other conditions mentioned.

The diagnosis of cerebral hemorrhage was suggested by the fact that the most outstanding symptom, the intermittent cyanosis, is also the most characteristic, in fact, practically a pathognomonic sign of subtentorial cerebral hemorrhage in premature infants. In such cases death almost invariably results, though in a few instances remarkable recovery has followed the withdrawal of bloody spinal fluid by lumbar puncture. The fact that normal, colorless spinal fluid was obtained in the case under discussion did not rule out the possibility that the symptoms were due to a hemorrhage sustained at birth, because by the end of thirty days, and probably sooner, the evidence of an extensive hemorrhage may disappear from the spinal fluid.

In patients presenting intermittent or paroxysmal cyanosis, blood clots are invariably found around the medulla oblongata at necropsy. The intermittent cyanosis may perhaps be explained on the basis of pressure by these clots affecting the respiratory or vasomotor centers or both.

REVIEW OF THE LITERATURE

In the literature on cerebral hemorrhage of the new-born infant I have been able to find the record of only one case that is similar to mine, in that death occurred late as a result of hemorrhage caused by an injury sustained at birth. This case, reported by Schule,[6] differs from mine in that the hemorrhage occurred just previous to death instead of at the time of birth, as in the case presented.

Schule's patient was a full-term infant who presented with the occiput posteriorly and was delivered by forceps after a prolonged labor. The birth weight was 3,760 Gm. (8 pounds, 5 ounces). There were no signs of asphyxia, but the child was somewhat drowsy during the first few days of life. This drowsiness, however, disappeared, and the infant nursed well and seemed normal in every respect until the age of 45 days. At that time, while resting, the child suddenly cried out, had a loose bowel movement, became pale and cyanotic and went into a state of collapse. There were no convulsions. Shortly afterward the left eyelid began to swell, the left globe protruded and the left pupil became wider than the right and reacted sluggishly to light. The right eye and pupil were normal. The anterior fontanel was tense and bulging. Two days later, the child died without developing any other significant symptoms.

At necropsy, there was a large subdural hemorrhage extending backward from the fissure of Sylvius and downward into the middle cranial fossa over the left cerebral hemisphere. The clot was uniform in color and apparently fresh, and was thickest (1 cm.), over the tentorium cerebelli and in the middle cranial fossa. There was no hemorrhage into the ventricles or into the brain substance. The

6. Schule, A.: Ein Fall von spät auftretender geburtstraumatischer Meningealblutung, Monatschr. f. Kinderh. **26**:43, 1923.

origin of the hemorrhage was explained by a rupture of the upper lamina of the tentorium, not involving the free edge but extending backward and into the sinus transversus. The leaves of the tentorium were infiltrated with blood.

Schule attributed the late onset of the hemorrhage to a defective repair of the original sinus tear at birth. This defective repair, he assumed, may have been ruptured by some increase of intracranial pressure, as in an intestinal cramp, which apparently accompanied the onset of cerebral symptoms in his case. On the basis of work by Wegefarth,[7] however, another explanation may be considered possible for the delayed onset of symptoms in Schule's case.

In order to demonstrate the fact that the pressure of the cerebrospinal fluid is usually greater than the pressure of the blood in the dural sinuses, Wegefarth made puncture holes in the walls of the superior longitudinal sinuses of dogs, thus establishing a communication between the sinus and the subarachnoid space. There was no hemorrhage into this space for at least four days, the duration of the experiments; although the openings in the sinuses remained patent.

Wegefarth's experiments may also explain the delayed onset of hemorrhage from a longitudinal sinus tear reported by Manton.[8] This case was that of a spontaneously delivered infant, aged 10 days, who had shown no evidence of intracranial injury at birth. The child died rather suddenly, and a fresh clot was found in the occipital region, the blood coming from a tear in the superior longitudinal sinus. It thus appears possible that death may not result from a sinus tear until some derangement of the intracranial mechanics produces in the dural sinuses a pressure higher than that exerted by the cerebrospinal fluid. It might even be possible, if this is true, that some cases of pachymeningitis hemorrhagica of infancy in which the patients recover or in which necropsies are not performed are instances of late cerebral hemorrhage resulting, for unknown reasons, at a period comparatively remote from the time of birth but as the result of injury sustained at that time.

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7. Wegefarth, P.: Studies on Cerebrospinal Fluid, J. M. Research **31**:149, 1914.

8. Manton, W. P.: Asphyxia Neonatorum and Its Sequellae, New York State J. Med. **14**:302 (June) 1914.

PSEUDOMEMBRANOUS ENTEROCOLITIS AND MASTOIDITIS ASSOCIATED WITH INFECTION WITH MORGAN'S BACILLUS *

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In his original work on summer diarrhea in London, Morgan [1] described a bacillus isolated from the intestinal contents in twenty-eight of fifty-eight cases, which was gram-negative, motile, a producer of acid and slight gas in dextrose, levulose and galactose broths, not reacting with the other sugars, and forming indol in peptone beef broth. The bacillus was demonstrated to be pathogenic when fed to rats and rabbits. Bacilli giving the same cultural reactions have since been reported by several others as associated with or causing enteritis. The agglutination reactions [2] have proved to be of little if any value in their identification, presumably due to the occurrence of different strains. The conclusion of Dick, Dick and Williams,[3] that the epidemic of enteritis associated with mastoiditis which they observed in infants was primarily an intestinal infection due to Morgan's dysentery bacillus, has prompted the report of the following case:

REPORT OF CASE

History.—F. C., a boy, aged 6 months, was admitted to the nursery ward of Lane Hospital on Sept. 4, 1927, for diarrhea, fever, vomiting and occasional attacks of cyanosis. The family history was unimportant. The birth history was normal, except that the baby was supposed to have been eight weeks premature and weighed 6 pounds (2.7 Kg.). He was breast fed for four days only, after which bottle feeding was begun because the breast milk "did not agree with the baby," as shown by frequent and sometimes forceful vomiting. At the age of three weeks, he was said to have had an attack of measles. On account of constipation and vomiting, various formulas were used including cow's milk, S. M. A. and Mellin's food, and for several weeks before the onset of the complaints at the time of admission, the baby had received a formula composed of dextrose maltose mixture and goat's

* Submitted for publication, Sept. 21, 1928.

* From the Department of Pediatrics, Stanford University School of Medicine.

1. Morgan, H. de R.: The Bacteriology of the Summer Diarrhea of Infants, Brit. M. J. **1**:908, 1906.

2. Kliger, I. J.: The Agglutination Reactions of the Morgan Bacillus No. 1, J. Exper. Med. **29**:531 (June) 1919.

3. Dick, G. F.; Dick, G. H., and Williams, J. L.: The Etiology of an Epidemic of Enteritis Associated with Mastoiditis in Infants, Am. J. Dis. Child. **35**:955 (June) 1928.

milk. This milk was obtained from two Toggenburg ewes owned by the parents. The baby's weights as remembered were 11 pounds (5 Kg.) at the age of 2 weeks and 10 pounds (4.5 Kg.) at the age of 4 months. Feeding of cereals had been begun when he was 4 months old and orange juice when he was 5½ months old.

Seven days before entry the baby had become ill; he had had irregular attacks of cyanosis of the head, hands and feet, fever and diarrhea. The diarrhea continued with the passage of from eight to twelve green stools a day, which contained mucus, curds and occasional flecks of blood. The private physician ordered tepid baths for the fever, which went as high as 106 F., soda enemas, soda and water by mouth, tablets containing a bismuth preparation, and a glucose and calcium caseinate formula. The child, however, had not retained any food for two days before admission. Both legs were burned by a hot water bottle the day before entry.

Physical Examination.—Examination showed that there was a fair amount of subcutaneous fat and slight evidence of dehydration. The weight was 9½ pounds (4,400 Gm.). There were many fine and coarse râles at the bases of both lungs, but no changes in the character of the breath sounds or in percussion. There were small, deep burns exposing about 1 and 2 sq. cm. of subcutaneous tissue on the right and left legs. There was an increased tonus of all the voluntary muscles. The head was held slightly back, though the neck was not rigid, and the back was slightly arched. Both membranae tympani appeared normal when the patient was admitted to the hospital (examined by the resident physician and me). The temperature was 38.6 C. (101.5 F.). The urine showed a light cloud of albumin, many hyaline casts and a few leukocytes. The blood count showed 68 per cent hemoglobin (Sahli), 8,250 white blood cells, 18 per cent polymorphonuclear leukocytes, 62 per cent lymphocytes and 21 per cent transitionals and large mononuclears. The Wassermann reaction of the blood was negative. The spinal fluid did not show an increase in the number of cells, and globulin was not present.

An irregular fever continued, ranging between 38 C. (100.5 F.) and 40 C. (104 F.) on September 6, and reaching 40.6 C. (105.5 F.) degrees on September 8. There were frequent regurgitations, and from ten to fifteen watery, greenish stools were passed a day. A culture of one stool was reported as negative for bacilli of the typhoid, paratyphoid and dysentery groups. On September 6, another specimen of urine did not show albumin, but moderate numbers of hyaline and granular casts were found. On September 7, the second white blood count was 7,500 with 34 per cent polymorphonuclear leukocytes, 46 per cent lymphocytes, 16 per cent transitionals and large mononuclears, 2 per cent eosinophils and 2 per cent basophils.

The infant became more dehydrated and was given two hypodermoclyses and one intraperitoneal infusion of physiologic salt solution. On September 7, examination showed that the right membrane tympani was slightly bulging posteriorly and slightly reddened and had a fair light reflex. The left membrana tympani was normal in position and color, with a fair light reflex. Incision of the right membrana tympani yielded purulent fluid. Death occurred on September 8 after a short period of irregular breathing.

Necropsy.—The necropsy, performed five and a half hours after death by Dr. E. V. Hall of the department of pathology, showed a small amount of mucopurulent exudate in the right middle ear and in the right mastoid antrum, considerable frothy fluid in the bronchi and a pseudomembrane in the lower part of the duodenum. The wall of both the large and the small intestine felt thickened, the latter being somewhat dilated. The mucous membrane of the jejunum was covered with a thick grayish pseudomembrane which was deeply bile-stained over

the surface. The mucous membrane beneath was much congested. In the lower part of the jejunum and ileum, there were patches of pseudomembrane. The lower part of the ileum was thickly covered, and Peyer's patches were swollen and deeply congested. The entire colon was covered with a thick pseudomembrane, and the mucous membrane in the cecum was almost completely atrophied, having a white fibrous appearance. The solitary follicles were prominent throughout the colon.

Histologic examination demonstrated extreme fatty infiltration of the liver; marked focal necroses of the malpighian bodies and marked congestion of the spleen; considerable granular swelling of the cells of the kidney tubules; a somewhat widened and slightly irregular epiphyseal line of the rib; practically no lipoid material in the suprarenal cortex, little in the medullary portion; thin septums with dilated alveoli in the lung, and heavy round cell infiltration of the mucosa of the small intestine with marked congestion of the submucosa.

The bacteriologic examination showed occasional gram-positive diplococci and semioccasional gram-negative, rod-shaped bacilli in the spleen; a great many gram-positive diplococci, a few large encapsulated gram-positive diplococci and a few thin, rod-shaped, gram-negative bacilli in the right middle ear and the right mastoid; a great many bacteria in the jejunum and ileum, including large gram-positive rods and large gram-positive, unpaired cocci, and many diplococci in the bone marrow.

Cultural studies of pus obtained from the ear at the time of paracentesis and of the heart blood at necropsy were made by Miss Ruth Wells, assistant in the bacteriological laboratory. Both yielded growths of gram-negative bacilli which gave the cultural reactions of Morgan's bacillus, and of nonhemolytic streptococci (Gamma of Brown).

COMMENT

While, unfortunately, cultures for Morgan's bacillus were not made from the stools or intestinal contents, there appears to be little doubt, judging by the positive cultures obtained from the middle ear and from the blood at necropsy and by the clinical development of the symptoms from an initial enterocolitis, that this case belongs to the same group as those of Dick, Dick and Williams. Here, too, the infection of the middle ear should be regarded as secondary to the intestinal infection, and not vice versa, since at the time of admission, when the diarrhea had already been present for several days, both tympanic membranes appeared normal, and abnormalities were not noted in either ear in spite of daily examinations until three days later. At this time, the observed changes were characteristic of a beginning otitis media.

This case also brings up another possible objection to, or risk in, the use of unsterilized goat's milk, since Morgan and Ledingham [4] found by experimental inoculation that the bacillus was markedly pathogenic for goats. The baby had subsisted on a diet which had in all probability been deficient in vitamin content, and this deficiency, according to the

4. Morgan, H. de R., and Ledingham, J. C. G.: The Bacteriology of Summer Diarrhea. Proc. Roy. Soc. Med. **2**:133, 1909.

animal experiments of Verder,[5] may have made the infant less resistant to one of the *paratyphoid-enteritidis* group of organisms to which Morgan's bacillus belongs.

SUMMARY

A case of pseudomembranous enterocolitis is presented in which the patient later developed the clinical evidences of infection of the middle ear, and in which Morgan's bacillus was isolated from the heart blood and from the middle ear.

5. Verder, E.: Effect of Diets Deficient in Vitamin A or B on Resistance to Paratyphoid-Enteritidis Organisms, J. Infect. Dis. **2**:589 (June) 1928.

Progress in Pediatrics

CONGENITAL DUODENAL STENOSIS AND ATRESIA*

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Although congenital obstruction may occur at any level or in any degree along the entire gastro-intestinal tract, we shall confine our discussion to congenital obstruction of the duodenum.

Practically all writers on this subject agree that Calder recorded the first case of congenital duodenal occlusion in the *Journal of Medical Essays,* Edinburgh, in 1733. Cordes [1] of New York, in 1901, reported fifty-seven cases including a case report of her own, this being generally accepted in the literature as the total number of cases reported to that year. On the contrary, we find that the oldest case in her record was that described in 1808 by Aubrey,[2] and that she entirely overlooked Calder's case as well as the case of Daniel reported in 1765 in which there was absence of the heart, lungs, liver, pancreas, spleen and left kidney in addition to the duodenal malformation.

In 1905, Little and Helmholz [3] reported twenty-seven cases of duodenal atresia in which the atresia was above the papilla of Vater. In checking this list closely with that of Cordes' [1] report of cases up to the year 1901, we find that Little and Helmholz [3] mentioned five cases which Cordes did not include. These five cases plus the two formerly mentioned added to Cordes' [1] list of fifty-seven make the number reported up to 1901 approximately sixty-four. From this time until 1912 practically all of the cases reported in the literature were listed by Spriggs [4] in his article on "Congenital Intestinal Occlusion" in *Guy's Hospital Reports* in which he mentioned ninety-two

* Submitted for publication, Dec. 26, 1928.

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1. Cordes, L.: Congenital Occlusion of the Duodenum, Arch. Pediat. **18**:401 (June) 1901.

2. Aubrey, H.: Med. chir. Zeitung **15**:269, 1808.

3. Little, H. M., and Helmholz: Situs Transversus and Atresia of the Pyloris, Bull. Johns Hopkins Hosp. **16**:249 (July) 1905.

4. Spriggs, N. I.: Congenital Intestinal Occlusion, Guy's Hosp. Rep. **16**:143, 1912.

cases of duodenal obstructive malformation. In 1919, Cautley [5] added eleven cases to the ninety-two collected by Spriggs, at the time rejecting three of those mentioned by Spriggs as doubtful, making the total number of cases reported up to 1919 about 100. As nearly as can be estimated, Garvin,[6] in searching the available literature in 1928, collected twelve cases reported during the period between 1919 and 1926. He referred to two cases reported by Schroder [7] and Smellie [8] each. On examining their articles, however, we find three cases each described bringing his total to fourteen.

Six more case reports are to be found in searching the literature during the period from 1919 to 1926 by the following authors: Denzer,[9] one; Stransky,[10] one, and Quinland,[11] four. This brings the total up to twenty cases, and added to the 100 cases reported up to 1919 brings the approximate total up to 1926 to 120. During the period from 1927-1928 including the case we are reporting, the case reports number nine: Veau and Hallez,[12] two; Thorndike,[13] six, and Garvin,[6] one, bringing the total number of cases reported from Calder's case in 1733 to our case at the present time to 129. Numerous other cases are mentioned in series in the literature that would increase the total number materially, but we have deemed it advisable to collect only those definitely reported.

Quinland [11] before reporting his two cases of malformation of the intestine became sufficiently interested to search the Warren Anatomical Museum of the Harvard Medical School for similar material, finding there the reports of twenty-five more unpublished cases, making twenty-seven in all. Four of these twenty-seven cases of malformation along the entire intestinal tract were duodenal atresias; there were no stenoses.

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5. Cautley, E.: Duodenal Stenosis, Brit. J. Child. Dis. **16**:65, 1919.

6. Garvin, J. A.: Congenital Occlusion of the Duodenum by a Complete Diaphragm, Am. J. Dis. Child. **35**:108 (Jan.) 1928.

7. Schroder, C. H.: Congenital Obstruction of the Duodenum, J. A. M. A. **78**:1039 (April 8) 1922; Diagnosis of Congenital Duodenal Occlusion, ibid. **82**:686 (March 1) 1924.

8. Smellie, J. M.: Three Cases of Congenital Duodenal Occlusion, Brit. J. Child. Dis. **21**:192 (July-Sept.) 1924.

9. Denzer, B. S.: Congenital Duodenal Obstruction: Malrotation of Intestine; Report of Case, Am. J. Dis. Child. **24**:534 (Dec.) 1922.

10. Stransky, E.: Congenital Stenosis of Duodenum Resembling Pylorospasm, Med. Klin. **18**:1433 (Nov. 5) 1922; abstr., J. A. M. A. **79**:2201 (Dec. 23) 1922.

11. Quinland, W. S.: Congenital Malformation of the Intestine, Atresia and Imperforate Anus: Report of Twenty-Seven Cases, Boston M. & S. J. **187**:870 (Dec.) 1922.

12. Veau, V., and Hallez, G. L.: Duodenal Stenosis in Infants, Bull. Soc. de pédiat. de Paris **25**:223 (March-May) 1927; Nourrisson **15**:244 (July) 1927.

13. Thorndike, Augustus: Duodenal Atresia and Stenosis in Infancy, Boston M. & S. J. **196**:763 (May) 1927.

Undoubtedly there have been many unreported cases of congenital duodenal malformation throughout the world. A search of the autopsy files at the Post Graduate Hospital for the past six years covering about 475 autopsies revealed no other case than the one we are reporting.

REPORT OF CASE

History.—G. M., a girl, born on April 12, 1928, was admitted to the hospital on May 5, at the age of 23 days. She was the only child. The family history was unimportant.

The child was born at full term by breech presentation, forceps being used on the after-coming head. She cried lustily immediately after delivery, took the breast well later and in every respect was a normal new-born child. The weight at birth was 6 pounds (2.7 Kg.), and there was no history of any disease prior to admission.

The child was entirely breast fed from birth, the breast being given every four hours the child nursing fifteen minutes. Water was given freely.

The chief complaint was vomiting. At the age of 3 days, she began vomiting her feedings and since then (twenty days) had vomited every feeding. Vomiting occurred from one-half to one hour after feeding; at times it was projectile in character, at others, a mere regurgitation. She lost 1¼ pounds (0.6 Kg.) since birth. There was marked constipation, the bowels moving only every two or three days and then only after use of a suppository. The stools were moderately firm in consistency and dark brown. A tentative diagnosis of pylorospasm with a possible pyloric stenosis was made.

Examination.—Physical examination presented three outstanding features: (1) an emaciated dehydrated infant; (2) peristaltic waves that traveled from the left upper to the right abdominal quadrant on stimulation, and (3) a suspicious mass which was palpable in the region of the pylorus. The heart and lungs were normal; the rest of the examination gave negative results.

Treatment and Course.—Immediately on admission the child was put on the breast every three hours, nursing twenty minutes at each feeding. Atropine, $\frac{1}{1000}$ grain (0.000065 Gm.), was given fifteen minutes before each feeding. There was a total cessation of the vomiting and a gain in weight from 4 pounds, 10 ounces to 5 pounds, 12 ounces. On the third day after admission the child began to vomit once daily, forceful in character, and only in small amounts. The weight on this day was 4 pounds, 12 ounces, a loss of 9 ounces in two days. Because the child was losing, and because it was assumed that the breast milk was inadequate, two teaspoonfuls of Dryco and 2 ounces of water were given after each breast feeding as a complementary feeding. At the same time the atropine was increased to $\frac{1}{500}$ grain (0.00013 Gm.) given fifteen minutes before each feeding. Vomiting continued once daily. During this period the child was having two small, soft yellow stools daily. The weight remained the same.

On the seventh hospital day, the infant began vomiting three or four times daily, occasionally projectile in character. Treatment continued the same. On the eleventh hospital day vomiting continued three or four times daily. The atropine was increased to $\frac{3}{1000}$ grain (0.00019 Gm.) given fifteen minutes before each feeding, and three teaspoonfuls of thick farina were given every two hours. On the fourteenth hospital day the same treatment was continued. Vomiting occurred four times daily, projectile in type. The weight was then 4 pounds and 10 ounces. At this time the infant was having one yellow soft stool. With the persistence of the vomiting and the gradual loss in weight, in the presence of a markedly

emaciated child showing marked visible peristalsis and the presence of a tumor mass in the right upper abdominal quadrant, the clinicians and surgeons felt reasonably sure that they were dealing with pyloric stenosis and deemed it advisable to operate. Due to the extremely poor condition of the patient a transfusion of 100 cc. of whole blood was made, being given by the Unger method.

On the fifteenth hospital day an exploratory laparotomy was performed, and no pyloric tumor was found. Nothing abnormal could be found by the surgeon, and after twenty-five minutes of careful exploration, the abdomen was closed. Following the operation the child vomited a dark brown fluid immediately after feeding. The atropine was increased to $\frac{1}{250}$ grain (0.00026 Gm.) before feedings, the child being fed every three hours as before.

On the sixteenth hospital day the child continued to vomit dark brown fluid after every feeding. The condition became weaker, and the respiration labored with an associated irregular fast heart. The child died at midnight.

Gross Observations at Autopsy.—The body was that of a poorly developed, undernourished, dehydrated female infant about 1 month old. There was practically no obvious postmortem change except a moderate rigor mortis. From the nose and mouth there was exuding a greenish-brown granular fluid with a decided fecal odor. There was a small incised wound about 1 cm. long over the right jugular; a similar incised wound over the left anticubital fossae, and a linear incised wound 6 cm. long running vertically just to the left of the umbilicus, closed with black sutures. None of the wounds showed gross infection or obvious healing. The body was 49 cm. long and weighed approximately 3 Kg.

The head was small; both anterior and posterior fontanels were open, the whole, however, giving the feeling of overriding of the sutures. The pupils were equal and regular and about 3 mm. in diameter. The cornea was grayish and glazed. The ears, nose and mouth appeared to be grossly normal.

There was a normal disposition of hair. No gross glandular abnormalities were noted. The skin felt dry with a loss of turgor and what appeared to be a decrease of subcutaneous fat. The skin was wrinkled and of a cyanosed hue.

When the abdomen was opened through the operative incision, there was no gross evidence of infection or healing. There was a short, thin omentum, while the coiled intestines showed fresh blood, which in some places began to clot, as evidenced by firm strands of fibrin. There was little free peritoneal fluid, chiefly serosanguineous in type.

The sigmoid colon appeared to be normal and contained dry yellowish fecal concretions. The rest of the colon appeared to be relatively normal except for a few scattered hemorrhagic areas and the fact that the transverse colon was adherent to the greater curvature by organized fibrinous tissue. The small intestine was very much the same. There were, however, two areas, one about the middle of the ileum, the other about the distal third of the jejunum, in which there was sharp kinking of the intestine with a few firm strands of fibrin binding the loops together. There was no occlusion of the lumen, however.

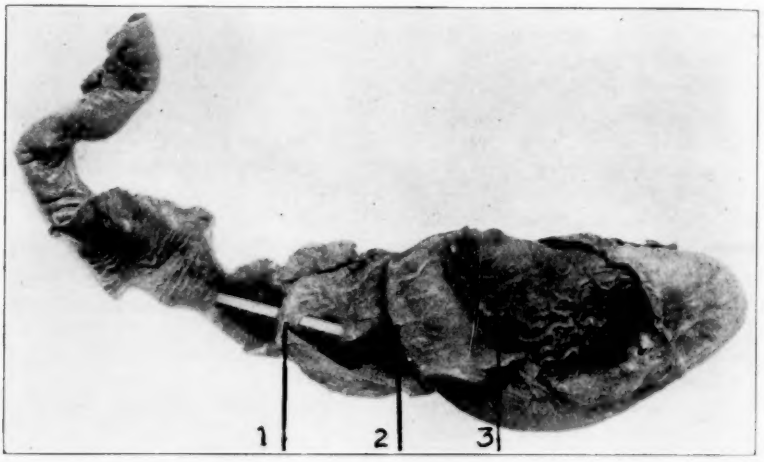
On removal of the stomach and duodenum, a dilatation of the stomach and the upper horizontal portion of the duodenum was noted. Below the dilatation a constricted area was felt which was hard. When the stomach was opened it contained a small amount of mucinous material and was considerably distended. It measured 10 cm. in length and 6 cm. in largest diameter. The pyloric ring measured 4 cm. in circumference. The wall of the stomach was everywhere thickened. The mucosa was swollen but had a smooth surface. The musculature of the pylorus formed a thick layer. Altogether the pylorus measured 6 mm. in diameter. The upper portion of the duodenum formed a cystic dilatation. About 2 cm. below the

pylorus there was a constriction where the lumen barely let the narrow probe through. The lumen measured about 2 mm. in diameter. The duodenum measured about 3 cm. in diameter, and the lining of it was everywhere smooth. There was striking contrast of the wall of the duodenum above and below the constriction. Above, the duodenal wall averaged 4 mm., below almost 2 mm. The septum that formed the constriction is covered with smooth mucosa on both sides.

The liver was free from adhesions, measuring 11 by 8 by 5 cm. On section, it had a slightly granular, yellowish-red tint. The gallbladder was normal in appearance, containing about 3 cc. of thick, green bile.

The spleen was dark red, moderately firm and on section showed no gross abnormality. It measured 5 by 3 by 1.5 cm.

Both kidneys showed fetal lobulation with attached suprarenal bodies. The left measured 4.5 by 2.5 by 2 cm., the other, 3.5 by 2 by 2 cm. The capsules stripped readily, and cross-section showed relatively normal structure and cortex-medulla ratio.



Specimen of stomach and duodenum, showing intramural stenosis of the duodenum. *1* indicates stenosis of duodenum admitting probe; *2*, pyloric ring distended, and *3*, stomach.

The ovaries and uterus appeared to be normal and of fetal type. The bladder appeared to be normal and contained no urine. The mesentery was studded with numerous small, hard nodes.

The thorax showed relatively no free liquid. There were no pleural adhesions. The lungs presented grossly hypostatic congestion with crepitation throughout. On section, frothy serosanguineous fluid was expressed.

The heart measured 3 by 2.8 by 2.5 cm., was pale throughout and had no adhesions. The foramen was closed. The initial cusps showed "blood sands."

The thymus was present; it measured 2 by 2 by 0.5 cm. and presented no gross abnormality.

The external genitalia and anus appeared to be normal.

Anatomic Diagnosis.—The anatomic diagnosis was congenital duodenal stenosis, status postlaparotomy and marasmus.

Microscopic Examination.—The muscle cells of the heart showed distinct striation. There was no fibrosis seen.

The lungs showed narrow air spaces. Many of them were filled up with cellular exudate. The capillaries were congested. The septums were thickened. There were also many pigmented large cells in the alveolar spaces.

In the spleen, the folliculi were large. The sinuses contained a great deal of hemorrhage. There was some fibrosis throughout.

There was marked vacuolization throughout the liver. The fat droplets had an even distribution throughout. The periportal spaces showed some infiltration of lymphocytes. There was also some congestion of the capillaries.

The structure of the kidneys was well preserved. The tubular lining consisted of swollen epithelium. There was considerable congestion of the vessels throughout.

The uterus had a uniform glandular lining. The glands of the cervix and fundus were similar.

The ovary showed various stages of unripe follicles.

Sections of the stomach and duodenum showed normal structure except for marked hypertrophy of the muscle layers above the constriction.

The diagnosis was congenital duodenal stenosis; status postlaparotomy; marasmus and bronchopneumonia.

COMMENT

Occurrence.—Cordes,[1] in quoting Theremin (*Deutsche Zeitschrift für Chirurgie*) wrote that this malformation is exceedingly rare, the records of the largest foundling asylums showing only isolated cases. The Vienna Foundling Asylum during the eleven years prior to 1901 had only two cases. In the St. Petersburg Foundling Asylum only nine cases were found, whereas no cases were recorded in similar institutions in Moscow up to and including 1901. St. George,[14] in 1918, reported that in the large necropsy service at Bellevue Hospital during the fourteen years prior to 1918 only two cases of congenital obstruction of the intestine were observed, one of which was duodenal.

Ralston,[15] in 1925, observed that not one of thirteen cases of congenital atresia or stenosis of the intestine collected by Barnard [16] from the records of the London Hospital was duodenal. At Booth Hall Infirmary, with 4,000 admissions of children yearly, there had not been a case during the period from 1916 to 1925.

Thorndike,[13] in 1927, found twenty-seven cases of atresia somewhere along the intestinal tract in 70,000 new-born infants in the Lying-In Hospitals in Boston, Chicago and New York. Thirteen cases of atresia in 301,541 new-born infants in the Lying In Hospital of Copenhagen. Petrograd and Vienna were reported by von Koos,[17]

14. St. George, A. V.: Congenital Intestinal Obstruction with the Report of a Case, Am. J. Dis. Child. **15**:355 (May) 1918.

15. Ralston, G.: Congenital Occlusion of the First Part of Duodenum, Brit. M. J. **2**:1005 (Nov.) 1925.

16. Barnard, H. L.: Contributions to Abdominal Surgery, James Sherrin, 1923, p. 144.

17. Von Koos, A.: Jahrb. f. Kinderh. **93**:240, 1920.

which with Thorndikes' series make a total of forty cases of atresia in 371,541 new-born infants. Von Koos [17] reported that 30 per cent of gastro-intestinal atresias are duodenal. His statistics are confirmed by Davis and Poynter [18] who, in 1922, collected 392 cases of congenital intestinal occlusion, of which 124 or 33 per cent were duodenal.

These observations lead one to the conclusion that this condition is not so rare as formerly thought.

Site.—The site of the defect is of interest. In cases collected by Pehu and Auberge [19] and Cautley,[5] the location was given in percentages as follows: proximal to papilla of Vater 40; opposite to papilla of Vater 7; distal to papilla of Vater 34; duodenal-jejunal juncture 5, and unclassified 14.

Garvins [6] figures of 113 cases changed to percentage by us for means of comparison vary considerably from the aforementioned especially in cases occurring at the duodenal-jejunal junction and opposite the papilla of Vater: proximal to papilla of Vater 34; opposite to papilla of Vater 19; distal to papilla of Vater 25; duodenal-jejunal juncture 19, and unclassified 16.

Congenital duodenal obstruction may be partial or complete. It occurs as a developmental malformation usually with a complete atresia or absence of one portion and rarely as a stenosis. The pathogenesis is complicated and interesting. The most plausible and generally accepted hypothesis is that it is due to congenital developmental malformation especially with reference to the type of case we are reporting. Bland Sutton [20] as early as 1889 said, "Congenital obstruction and narrowing of the alimentary tract are always found in the situation of embryological events."

In 1901, this was refuted by Cordes [1] who said that the statement "was not strictly correct as occlusion of the intestinal tract can take place at any point, often without reference to special embryological events"; however, the majority of subsequent investigators and writers have failed to support Cordes' theory.

The formation of the duodenum, pancreas and liver in the fetus all occur at one sector in the gastro-intestinal canal. The fetal liver and pancreas are forming at the same time as buds from the digestive tract. It is important to notice that such complex and vital structures are budding in close proximity as well as the intricate vascular system that is developing simultaneously to be enmeshed as their nutrient supply.

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18. Davis, D. L., and Poynter, C. W. M.: Congenital Occlusions of the Intestines, Surg. Gynec. Obst. **34**:35, 1922.

19. Pehu, M., and Auberge, A.: Retrecissements congenitaux du duodenum. Arch. de méd. d. enf. **27**:330, 1924.

20. Sutton, J. Bland: Imperforatedileum, Am. J. M. Sc. **98**:457, 1889.

Any deviation from the normal mode of development of these structures would result in a serious maldevelopment of the first part of the intestine.

During the fourth to fifth week of fetal life, the duodenum is occluded by an epithelial proliferation. Normally, this should absorb and restore the lumen. It is logical to assume that in maldevelopment of the viscera or their vascular supply, this epithelial proliferation might not absorb at all or might only partially absorb, producing a partial or complete occlusion. An occlusion of this type and an accompanying vascular maldevelopment with secondary necrosis at this point may be the etiologic factor of complete duodenal occlusion. Stenosis might be explained by taking a completely occluded lumen with only a partial defect in the vascular development producing a canalized lumen. The degree and length would vary according to the degree of anomalous development.

Various theories have been offered by other writers, such as volvulus, fetal peritonitis, ulceration, pressure by new growths, abnormally long persistence of the omphalomesenteric artery, traction due to inguinal hernia and embolism of the superior mesenteric artery. It is folly to try to explain all types of duodenal malformations at all locations by any one theory. It appears to us, however, that the intramural type of congenital duodenal obstruction is best explained by the viscerovascular maldevelopment theory already described; the etiology of the extramural type is evident.

Any type of obstruction may occur, from partial to complete absence of a portion of the bowel. Little and Helmholz [3] did not recognize this, stating that in no case was there a complete absence of a portion of the bowel but merely an obliteration of the lumen for a longer or shorter distance. They further stated that all cases had in common some lumen connecting the proximal and distal portions of the duodenum. They stated that had the number of cases in which the connection was described as a strand of fibrous tissue been subjected to microscopic examination, there would have been found a small lumen lined by epithelium representing a much constricted and atropic portion of the bowel. This was proved erroneous by Cockaye [21] in his case in which there was a complete interruption in continuity of the two portions microscopically. It seems plausible that, considering embryologic development with the infinite number of developmental pitfalls possible, one could explain almost any form of duodenal obstruction from a microscopic indenture in the lumen to a condition in which both portions are completely interrupted with plausible hypotheses regarding etiology.

21. Cockaye, E. A.: Case Report of Congenital Duodenal Obstruction, Brit. J. Child. Dis. **14**:188 (July-Sept.) 1917.

The majority of the authors of the larger collection of cases regard from 5 to 7 per cent as a fairly accurate estimate of the occurrence of other malformations accompanying obstruction of the duodenum; however, Cordes [1] found eleven cases in her fifty-seven. Accompanying anomalies included imperforate anus, entire absence of one or more organs and other atresias or stenoses occurring anywhere along the gastro-intestinal tract from the esophagus to the anus.

The discovery of the second anomaly is often of utmost importance. Kirmisson [22] reported a case of a baby who had been operated on for anal stenosis soon after birth "with apparent success"; however, the infant resumed vomiting and died. Necropsy showed a valvular obstruction of the duodenum in addition to the anal defect. In Markwald's case there was atresia of the esophagus and rectum coexisting with the duodenal maldevelopment. Thorel's [23] case had seven points of atresia. Little and Helmholz's [3] case was unique in that there was complete absence of the pylorus and duodenum as far as the ampulla of Vater.

SYMPTOMS AND SIGNS

Vomiting was present in every case reported. It began either at birth (which was noted in the greater majority of the cases) or on the second to the fifth day after birth. Its nature was forceful or projectile, depending on the degree of the obstruction and the tonicity of the gastric musculature. The vomiting occurred in some cases only once in twenty-four hours, while in others, it occurred after every feeding. In some cases the inanition was so marked and the gastric musculature so atonic that the stomach would dilate to a considerable extent, holding from three to four feedings before it would have the ability to express it.

The vomitus is bile-stained or not depending on whether the obstruction is proximal or distal to the ampulla of Vater. When proximal, the vomitus usually consists of whatever has been ingested or, if no food has been taken, is of a mucous-like appearance varying from a whitish froth to a light brown. When distal, the vomitus is greenish. A few writers speak of bile-stained material in the vomitus when the obstruction was proved to be proximal to the common duct. These were proved at autopsy to have an anomalous bile duct emptying into the duodenum above the obstruction. Some regard the vomiting of amniotic fluid soon after birth as pathognomonic of high congenital obstruction. Hematemesis is rare.

The chemistry of the vomitus except for the determination of the presence or absence of bile is of no assistance.

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22. Kirmisson, E.: Traité des maladies chirurgical, 1898, p. 412.

23. Thorel, F.: München. med. Wchnschr. **46**:1202, 1899.

The stools should be examined for the presence of bile, for if there is bile in both the stool and the vomitus, either the obstruction is not complete or there are two openings of the common duct into the duodenum. The persistent absence of bacteria in the meconium might help in diagnosing complete occlusion.

Constipation is marked; if the obstruction is complete or nearly so, constipation is absolute. The stools are usually extremely small.

Most cases present a picture of emaciation, and there is usually a progressive loss of weight varying with the degree of pathologic change. If the child lives long enough, there are usually starvation stools.

In fifty-five case reports that mentioned visible peristalsis, it was present in 62 per cent of the cases. It was markedly present in our case.

A tumor mass may or may not be felt. When present, it is felt as a large soft tumor in the right upper quadrant of the abdomen, and if the accompanying symptom-complex is present, it is usually conclusive evidence. It is a dilated proximal loop of duodenum. The palpation of this tumor is described by St. George [14] as Nothnagel's phenomenon, but he gives no reference.

The distention of the abdomen is great and high if present and is due to the dilated stomach and duodenum.

The x-ray picture is often helpful in arriving at a diagnosis. A combination of the roentgenogram and the fluoroscope should be used, and the patient should be examined in both the erect and the prone positions. Cases of duodenal obstruction have been missed only when the former position was used or vice versa. This should be resorted to early with the first suspicion of an obstruction. Bosch and Schinz [24] described the procedure in detail.

Chemical examination of the blood is helpful; that is, in obstruction there is a lowering of the chlorides and an increase of the carbon dioxide combining power.

Neff and Haden [25] spoke of the lowering of the chlorides as representing a protective mechanism, since the toxemia can be prevented in dogs with high intestinal obstruction if the chlorides are kept at or near the normal level. The therapeutic use of chlorides has been found to be of value experimentally both in animals and in human beings by Haden and Orr [26] after toxemia has well developed. On this hypothesis many men use and favor sodium chloride therapy as a pre-

24. Bosch, E., and Schinz, H. R.: Symptoms of Congenital Duodenal Stenosis as Seen in Roentgenogram, Deutsche Ztschr. f. Chir. **159**:284, 1920.

25. Neff, F. C., and Haden, R. L.: Congenital Transduodenal Bands, Am. J. Dis. Child. **30**:82 (July) 1925.

26. Haden, R. L., and Orr, T. G.: Use of Sodium Chloride in Treatment of Intestinal Obstruction, J. A. M. A. **82**:1515 (May 10) 1924.

operative and postoperative measure. The aforementioned authors [27] believed that the low chloride level is due to obstruction and not vomiting, basing their theory on experimental work done in cases of intestinal obstruction in human beings and in a monkey in the absence of vomiting, in dogs before vomiting began and in the rabbit, an animal which never vomits.

A low chloride blood level is also found in cases of cutaneous burns, roentgen-ray intoxication, serum sickness and pneumonia. We feel that the common factor in these widely different clinical conditions showing strikingly similar chemical changes is a protein split product intoxication of unknown origin. In all these conditions, there is an accelerated protein catabolism with high nitrogen and low chloride excretion and a high nonprotein nitrogen content in the blood.

The urine may or may not show acetone bodies, substantiating the experimental observations of Davis, Haldane and Kennaway who, in 1920, showed that acetonuria may occur with alkalosis. Many of the recent cases of duodenal obstruction have shown this.

DIFFERENTIAL DIAGNOSIS

In the differential diagnosis of congenital duodenal obstruction two things are to be considered: first, obstruction lower down, and second and most important, hypertrophic pyloric stenosis.

In obstruction lower down, the vomiting usually occurs at a longer interval after the ingestion of food. Schwalbe [28] noted that in high obstruction, the stomach was usually distended with retraction of the lower part of the abdomen, whereas in low obstruction, the abdomen protrudes. No tumor is felt in low obstruction. The x-ray picture should make the differential diagnosis absolute. Vomiting in duodenal obstruction starts either immediately after or within the first five days after birth in 90 per cent of the cases, whereas in the majority of cases of pyloric stenosis the vomiting starts during the third week. The character of the vomitus is especially helpful if it contains bile in appreciable quantities. The study of the meconium or stools for bile is again extremely helpful.

There may or may not be a tumor in either case, but when present, the pyloric tumor is usually a small gristly tumor giving a button-like

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27. Haden, R. L., and Orr, T. G.: Experimental High Intestinal Obstruction in the Monkey, J. Exper. Med. **41**:107, 1925; The Distribution of Chlorides in the Blood of the Dog After Experimental Intestinal Obstruction, ibid. **41**:113, 1925; The Sodium Content of the Blood of the Dog After Experimental Intestinal Obstruction, ibid. **41**:117, 1925.

28. Schwalbe, E.: Morphologie der Missbildungen des Menschen und der Tiere, 1909.

feel compared with the larger more boggy type of tumor of the duodenum.

The general emaciated appearance of the child with persistent loss in weight as well as visible peristalsis, if it is present, is the same in both cases. Jaundice if present points to duodenal malformation. The x-ray picture should be able to help materially, especially if Bosch and Schinz' technic is used. The blood chemistry does not help in differentiating, the chloride content being low and nonprotein nitrogen and carbon dioxide combining power increased in both instances.

Schroder [29] mentioned a procedure that has helped him establish a diagnosis of duodenal obstruction and at the same time rule out pyloric stenosis. This consists in passing a small catheter and washing the stomach until the return is clear. Following this the tube is pushed into the duodenum; if there is an obstruction, there is a characteristic gush of bile-stained fluid. If pyloric stenosis is present, the tube cannot be passed into the duodenum.

It seems to us that this procedure could be of no value when the obstruction is proximal to the ampulla of Vater (which it is in from 30 to 40 per cent of cases), especially if it is complete or nearly so; however, it is worthy of trial.

The treatment is surgical, a gastro-enterostomy or a duodeno-jejunostomy being indicated whenever it is possible. Careful preoperative and postoperative care is essential. Hypodermoclysis or peritoneal injections of saline or dextrose should be used, varying with the degree of dehydration. Feeding and use of stimulants vary so with each case that it is not possible to lay down a general rule governing these phases of the treatment.

Clogg [30] suggested that whatever operative procedure is used, the collapsed intestine distal to the obstruction should be gently inflated by water or air at operation. Not only has this been successfully done in a number of instances, but it makes anastomosis easier to perform and shows whether or not any further obstructions are present.

The prognosis is grave in lieu of the fact that the condition is frequently not thought of or the patient is not operated on until it is a most hazardous surgical risk. A more general and widespread consideration of the possibility of congenital duodenal obstruction in cases of obstructive vomiting during the first weeks of life will bring these patients to the operating table earlier with a resulting lowered mortality. Again when, as in our case, nothing to account for the vomiting is found when the abdomen is opened, the surgeon should keep in mind the possibility of an intramural obstruction.

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29. Schroder (footnote 7, second reference).

30. Clogg, H. S.: Congenital Intestinal Atresia, Lancet **2**:1770, 1904.

The only case reported in which the patient was cured was that of Ernst [31] who, in 1916, operated on a boy, aged 10 days, who had a congenital duodenal stenosis; a duodeno-entero-anastomosis was performed. Eleven months later, the child was a vigorous, well developed youngster. We have purposely omitted mentioning cases of extrinsic pressure such as peritoneal bands. Schroder [29] spoke of a case in which the patient was successfully operated on by a Dr. Abel, but he gives no references.

Hutchinson, in discussing the paper of Dr. Jewesbury and Dr. Page [32] on the treatment of duodenal obstruction by operation, referred to a case of duodenal stenosis in which the patient was operated on by Higgins, a gastro-enterostomy being performed successfully on a child, 1 week old.

Grulee [33] stated that four patients with congenital intestinal occlusion had been successfully operated on up to 1926; however, he does not specify the sites of obstruction.

We know of one other successful gastro-enterostomy performed by a New York surgeon in the case of an infant to relieve a congenital duodenal obstruction. A report will be found in the literature in the near future. Many unsuccessful cases have been reported.

The length of life is dependent on the degree of atresia or stenosis, most of the patients dying during the first ten days of life. Many lived longer, and there are cases of congenital stenosis in which the patient reached adult life, the most recent having been reported by Nagel.[34] The earliest death reported was one occurring thirty hours after birth. No patient with atresia has lived longer than thirty days without surgical intervention. Buchanan's case was interesting in that the patient lived eighteen months, and on autopsy a partial duodenal septum was found, the aperture of which was so small that it barely admitted the end of an ordinary probe.

SUMMARY

1. The condition in the case herein reported was diagnosed during life as pyloric stenosis.

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31. Ernst, N. P.: A Case of Congenital Atresia of the Duodenum Treated Successfully by Operation, Brit. M. J. **1**:644, 1916.

32. Jewesbury, R. C., and Page, Max: Two Cases of Duodenal Obstruction in Infants Treated by Operation, Proc. Roy. Soc. Med. (Soc. Dis. of Child.) **16**:50 (June) 1923.

33. Grulee, C. G.: Clinical Pediatrics, New York, D. Appleton & Company, 1926, vol. 3, p. 151.

34. Nagel, G. W.: Unusual Conditions in Duodenum and Their Significance: Membranous Obstruction of Lumen, Diverticula and Carcinoma, Arch. Surg. **11**: 529 (Oct.) 1925.

2. Laparotomy and exploration failed to reveal pyloric stenosis or any visible pathologic change which would explain the coexisting symptoms.

3. Intramural duodenal stenosis was found on postmortem examination.

4. Duodenal stenosis or atresia, we believe, is more common than formerly thought.

5. Congenital duodenal stenosis or atresia should be considered in any case of persistent vomiting of an apparently obstructive type during the first weeks of life or in any case presenting an atypical picture of the symptom-complex of pyloric stenosis.

Pediatric Biographies

FRANCIS GLISSON
1597-1677

JOHN RUHRÄH, M.D.
BALTIMORE

It has always seemed strange that rickets was not called Glisson's disease, in place of the English disease or any of the other names which it frequently bears. Certainly there are few monographs on any disease so complete and so thoroughly satisfactory.

The main facts of Glisson's life may be briefly stated. He was the second son of William Glisson, and was born at Rampisham in Dorsetshire in 1597. He was sent to Caius College, Cambridge, in 1617, receiving his B. A. in 1621, and his M. A. in 1624; he was incorporated M. A. at Oxford in 1627. Cambridge conferred the degree of M.D. on him in 1634. The next year he was elected a member of the Royal College of Physicians and was made regius professor of physic at Cambridge, which chair he held until his death although he appointed Dr. Brady his deputy professor two years before he died. He lectured on anatomy at the College of Physicians and in 1640, he delivered the Goulstonian lectures. For these lectures, which were given on three consecutive days, three diseases being discussed, one of the four younger doctors was chosen. He received 10 pounds and the dissector 2 pounds. Glisson was the second lecturer of which there is any record.

He practiced medicine about this time in the parish of St. Mary's at the Walls in Colchester. He was in the town in the siege of 1648, and was chosen by the Royalists to confer with Lord Fairfax, but his interviews were of no avail. As the town had suffered so severely in the siege and was so poor, Glisson, although his house remained standing, made up his mind to quit the place and set up in London. Here he was among the leaders in both medical and scientific matters, and was of the group whose meetings resulted in the founding of the Royal Society of which he was one of its first Fellows. He was also active in the affairs of the Royal College of Physicians, being censor in 1656 and president in 1667, 1668 and 1669. He died in London on Oct. 14, 1677, and was buried in the Parish Church at St. Bride, Fleet Street. His portrait, painted when he was 75, may be seen in the College of Physicians.

One must read between the lines of this skeleton outline of the master's life. It was a busy one and his great work on rickets was his

DE

RACHITIDE

SIVE

MORBO PUERILI,

qui vulgo

The **Rickets** dicitur,

Tractatus;

Operâ primò ac potiſsimùm

FRANCISCI GLISSONII

Doctoris & publici Profeſſoris Medicinæ in almâ *Cantabrigiæ* Academiâ, & Socii Collegii Medicorum *Londinenſium*, conſcriptus:

Adſcitis in operis ſocietatem

GEORGIO BATE,

&

AHASUERO REGEMORTERO

Medicinæ quoque Doctoribus, & pariter Sociis Collegii Medicorum Londinenſium.

LONDINI,

ypis *Guil. Du-gardi*; Impenſis *Laurentii Sadler*, & *Roberti Beaumont*: apud quos veneunt in vico vulgò-vocato Little Britain 1670.

Title page of the first edition of Glisson's book on rickets.

greatest contribution to medicine, but one must not forget his "Anatomia hepatis" (1654), nor the "Tractatus de natura substantiae" (1672), nor "Tractatus de ventriculs et intestinis" (1677).

"De rachitide" appeared in 1650. It was the first important contribution on the subject, which is strange because the disease must have been very common. Perhaps this may be the reason that it was overlooked, just as the common cold has never received the attention it so richly deserves. The picturesque Daniel Whistler had published five years before a little book on the subject (See "Pediatrics of the Past" for a disucssion of this and other points in connection with rickets and Glisson's book), and there were one or two other references to the disease.

The work was done in collaboration with seven other members of the College of Physicians who aided Glisson, Bâtes and Regemonter, who had been appointed by the College to collect and edit the papers on the subject. They go on to state:

> But when Dr. Glisson in the judgement of the rest, had accurately interweaved his part (which comprehending the finding out of the essence of this disease) and in that he had propounded many things different from the common opinion of Physitians (though perhaps the less different from the truth) we altered our Resolutions, and committed the first stuff of the whole work to be woven by him alone, least at length the part should arise deformed, misshapen and Heterogeneous to themselves.

The complete work appeared in 1650 in Latin, and was translated into English by Philip Arnim. It was then enlarged and corrected by Nicholas Culpepper Gent.

"De rachitide" is rather tedious reading, for it is verbose and written in the ponderous argumentative style of the day, but the facts are there and little or nothing has been added to the knowledge of the subject since, except by methods of research which were not available at that time.

Only one quotation may be given. If Whistler is omitted, this was the first description of the disease.

THE SIGNS OF THE PRESENT DISEASE OF THE RACHITES NEWLY BEGUN

First, *Diligent Observation must be employed about the three kinds of Signs ascribed above to the Animal Actions;* namely, the looseness and softness of the parts, the weakness and languidness, the slothfulness and numness. For these do in a remiss degree, and subobscurely yield advantage to circumspection and heedfulness presently a *principio principiant,* as they phrase it.

Secondly, *The colour must be considered, and the habit of the Head and Face in relation to the Joynts.* For if the colour or the habit be more fresh and lively in those than in these, it presenteth a strong suspition that this Disease hath taken root. For although the Bulk of the Head which is evidently encreased, and also

the extenuation of the parts affected do pre-require some considerable motion and duration of the Disease before they appear, yet from the beginning a certain difference may be observed by an accurate attention or intuition in respect of the heat and the habit of these parts compared one with another.

Thirdly, *The Wrists and the extremities of the Ribs must be noted.* For before the end of the beginning certain rudiments of knurls or knots begin to appear in the Wrists, and Excrescencies also in the tops of the Ribs.

Fourthly, A kind of swelled fulness and stretching *the Belly* is conspicuous immediately after the beginning, especially in the *Hypochondriacal* parts. For the magnitude of the Belly compared with the magnitude of the Breast exceeds the just and due proportion.

Now these Signs collectively taken do assuredly demonstrate the presence of the Disease even from the very beginning. But if no sensible and manifest extenuation of the first affected parts do appear at the same time, in that very respect it is cleerly distinguished from the encrease thereof.

Another extract is as follows:

These, our Anatomical Observations are distinguished into those which do extrinsecally occur, the Body being not yet opened, and those which present themselves only upon the Dissection of the Body.

I. THOSE OF THE FORMER KIND ARE THEY WHICH ARE OUTWARDLY VISIBLE UPON THE FIRST APPEARANCE OF THE NAKED DEAD BODY

1. An irregularity, or disproportion of the parts; namely, The Head bigger than ordinary, and the Face fat & in good constitution in respect of the other parts. And this indeed hath appeared in all those whom hitherto we have beheld to perish by this affect, one onely excepted, who together with this Disease had suppurated Lungs, and was pined and disfigured with the Ptysick. Yet he also throughout the whole progresse of the Disease, was full faced, and had his head somewhat big; but for about fourteen dayes before he Deceased, on a sudden all the fleshy parts about his head consumed away, and his face was like the picture of *Hypocrates,* not without the just wonder of all those who beheld so sudden a change.

2. The external members, and the muscles of the whole Body were slender and extenuated, as if they had been wasted with an Atrophy, or a Consumption. This (for so much as we know) is perpetually observed in those that die of this Disease.

3. The whole Skin, both the true, and also the fleshy and fattish Membrane, appeareth lank and hanging, and loose like a Glove, so that you would think it would contain a far greater quantity of flesh.

4. About the joynts, especially in the wrists and ankles certain swellings are conspicuous, which if they be opened, not in the fleshy or membranous parts, but in the very ends of the bones, you may perceive them to be rooted in their appendances; and if you will file away those prominencies of the bones, you will easily perceive them to be of the same similarly substance with the other parts of the bones.

5. The articles or joynts, and the habits of all the external parts are less firm and rigid, and more flexible then at another time they are observed to be in dead bodies; and in particular the Neck after death is scarce stiff with cold, at least much less then in other Carkasses.

6. The Brest is outwardly lean, and very narrow, especially under the arms, and seemeth on the sides to be as it were compressed, the Stern also is somewhat pointed, like the Keel of a Ship, or the brest of a Hen.

7. The top of the ribs to which the stern is conjoyned with gristles, are knotty, like unto the joynts of the Wrists and Ankles, as we have already said.

8. The Abdomen indeed outwardly in respect of the parts continent is lean, but outwardly in respect of the parts contained it is somewhat sticking out, and seemeth to be sweld and extended. And these have been our Observations before the opening of the bellies.

News and Comment

UNIVERSITY NEWS

Gift to Yale.—President Angell of Yale University announced on February 19, that the General Education Board, New York, had given $2,000,000, for a medical and pediatric laboratory and for a dispensary and service unit on the grounds of the New Haven Hospital, which is affiliated with Yale University School of Medicine.

CORRECTION

In the article by Dr. Adrien Bleyer, "A Clinical Study of Enuresis" (AMERICAN JOURNAL OF DISEASES OF CHILDREN **36**:989 [Nov.] 1928), the decimals in the last paragraph but one on page 996 are incorrectly given. The third sentence in this paragraph should read:

It is necessary in the use of atropine, for the cure of enuresis, to get the dosage as near the margin of overdosage (flushing, mydriasis) as is possible, and in this study a solution of one quarter of a grain to the ounce rather than one grain to the ounce was used, because a closer adjustment of the drug to the individual need could in this way be secured, each drop representing about one two thousandth of a grain instead of one five hundredth of a grain.

Obituary

CLEMENS VON PIRQUET, M.D.

1874-1929

On March 1, 1929, the world was shocked to learn of the tragic death of Dr. Clemens von Pirquet, professor of pediatrics at the University of Vienna. Pirquet was born in Hirschstetten, near Vienna, on May 12, 1874, the son of Peter Freiherr von Pirquet. He attended the Universities of Vienna and Graz. He was assistant to Professor Escherich from 1901 to 1908, and professor of pediatrics at Johns Hopkins University in Baltimore from 1908 to 1910, at the University of Breslau from 1910 to 1911 and at the University of Vienna from 1911 to 1929.

Pirquet, whose name is well known not only to pediatricians, but to every physician in the world, acquired his international fame, in the first place, through his discovery of the cutaneous tuberculin test. This test not only was a new diagnostic method for tuberculosis in childhood, but also afforded the possibility of studying the pathogenesis and many other questions of tuberculosis. The present knowledge of tuberculosis, to a great extent, has its foundation in studies made possible by the Pirquet test.

But this test was only a by-product of his great discovery in biology —the allergy. The changed reactivity of the organism by repeated introduction or invasion of pathogenic substances and germs revolutionized the conception of the time of incubation and of immunity. Allergic phenomena are encountered in almost all diseases. Pirquet's studies concerning serum sickness and vaccination are classic. The studies of asthma, hay-fever, eczema and different kinds of idiosyncrasies were especially benefited by the introduction of the conception of allergy. The tuberculin reaction stimulated the discovery of other cutaneous and intracutaneous tests, for instance, those for diphtheria, scarlet fever, trichophytosis and malleus.

During the last years of his life, Pirquet studied the mortality statistics of England, and on the basis of this study, which he had almost completed at the time of his death, he extended the term allergy to include changes in the reactivity of the organism in different age periods —a promising and highly interesting conception.

He published a study concerning the distribution of the rash in measles, and developed, on the basis of this study, a theory concerning the rash in measles and smallpox.

CLEMENS VON PIRQUET, M.D.

A great part of Pirquet's life was devoted to the development of a new system of nutrition, called the Nem System, the basis of which was formed by biometric studies. His study of the relation of the sitting height to other measurements of the body gave him the idea to use the sitting height square as the nutritional surface on which to calculate the food requirement. In his system, Pirquet substituted for the calorie a new unit, 1 cc. of human milk.

Pirquet's charming personality, his intelligence and his excellent knowledge of foreign languages helped to increase his international reputation. The United States of America honored him at the age of 34, with an appointment as professor of pediatrics at the Johns Hopkins University in Baltimore, where he made the plans and started the new building, the children's clinic. In spite of his return to Europe to fill the position of professor of pediatrics at Breslau, and shortly thereafter at Vienna, his association with the United States continued to be close. When, therefore, after the termination of the World War the American Relief Administration, under Hoover's leadership, started its immortal work for the starving Austrian children, it was to Pirquet that the organization of this undertaking was entrusted. In the feeding of 400,000 children daily, Pirquet was able to demonstrate the value of his system of nutrition. Likewise, the Rockefeller Foundation, which after the war helped the Universities of Austria in such a generous way, with full confidence in Pirquet, placed him in control of the endowment. The Commonwealth Fund and the Society of Friends were also in close contact with him.

Pirquet's death is a great loss, not only for pediatrics, but for the entire medical field. His clinic in Vienna, one of the most beautiful children's clinics in the world, was especially appreciated by physicians of the United States, many of whom received their pediatric education and inspiration through their study in this clinic. Many of the physicians had the opportunity to come into personal contact with Pirquet, whose home was always open to visitors from the United States. I am sure that all American physicians who came in touch with this great teacher and scientist, will always keep his memory alive and in the highest esteem. No words can describe what we, his close friends and pupils, have lost by his death.

B. S.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

OBSERVATIONS ON RETICULO-ENDOTHELIAL CELLS IN SEPTIC JAUNDICE. I. SHERMAN, Arch. Path. **7**:78 (Jan.) 1928.

A child, aged 11 days, had a temperature of 101 F. and was deeply icteric. There was a definite erysipelas on the face, and a blood culture gave 300 colonies of *Streptococcus hemolyticus* in 1 cc. The child died in twenty-four hours. At autopsy an excessive phagocytosis of streptococci was observed. Kupffer cells, capillary endothelial cells of the suprarenal glands and reticulum cells of the spleen and the bone marrow participated electively in the phagocytosis. In the absence of any obstruction of the bile ducts, as well as of lesions in the cells of the liver, the jaundice was thought to have been caused by severe impairment of the Kupffer cells.

SANFORD, Chicago.

THE BACTERIAL FACTOR IN THE RHEUMATIC INFECTIONS OF CHILDHOOD. CAREY F. COOMBS, M. J. & Rec. **127**:465 (Nov. 21) 1928.

Lesions produced in animals by experimental inoculation with streptococci derived from persons with rheumatic infection do not conform exactly to those of the disease as it is observed in man. One must realize, of course, that the constancy of rheumatic infection in the child depends largely on the circumstances under which it occurs, and hardly at all on the individuality of the micro-organism itself. This factor accounts for the differences observed between the experimental and the clinical lesions. In the child the infection appears in a continuous stream of doses, while in the animal it is introduced at one blow. In the child the organism enters through a mucous membrane and undergoes modification, while in the animal it enters directly into the circulation.

WILLIAMSON, New Orleans.

COLOR TESTS FOR VITAMIN A: THEIR APPLICATION TO NATURALLY OCCURRING PRODUCTS. S. G. WILLIMOTT and FRANK WOKES, Lancet **2**:8, 1927.

The relative sensitiveness of the four color tests for vitamin A—arsenic chloride (Kahlenberg's reagent), concentrated sulphuric acid (Drummond and Watson), powdered phosphorous oxide (Fearon), trichloracetic acid alone (Rosenheim and Drummond) or with pyrogallol or other polyphenols (Fearon), and antimony trichloride (Carr and Price) — were studied under parallel conditions and these were compared with feeding experiments. Vitamin A was completely destroyed in a potent cod liver oil after two hours with a mercury vapor quartz lamp at a distance of 3 inches. When the course of destruction was determined by means of the four tests, the arsenic chloride and antimony trichloride tests seemed most sensitive, then the concentrated sulphuric acid and phosphorus oxide tests, and last the Fearson's trichloracetic acid and pyrogallol tests. It was observed that destruction of the vitamin continued after the oil had been removed from the action of the rays.

It is probable that vitamin A is not identical with any of the four photosynthetic pigments, which interfere, however, with the color tests. Present evidence both by feeding experiments and by color tests indicates that vitamin A is not absorbed to any considerable extent by the charcoal used to remove carotin and xanthophyll. The color tests for vitamin A are not qualitatively interfered with by the presence of vitamin D. The oil of fresh orange rind is one of the most potent sources of vitamin A in the vegetable kingdom. Spinach leaves are also potent.

THE p_H AND ALKALINE RESERVE IN AVITAMINOSIS C. G. MOURIQUAND, A. LEULIER and P. SEDALLIAN, Compt. rend. Acad. d. sc. **185**:551, 1927.

The questions studied were: Does acidosis exist in the course of experimental scurvy and are the symptoms in scurvy due to acidosis? A determination of p_H in various stages of scurvy failed to show a condition of acidosis. After the twenty-seventh day of experimental scurvy, the alkaline reserve fell irregularly to about one third of its normal value by the fortieth day. The addition of bicarbonate, citrate and lactate to the ration does not influence the evolution of scurvy, and the lesions are not a function of acidosis.

EXPERIMENTAL RESEARCHES ON THE BIOCHEMISTRY OF SCURVY. GEORGES MOURIQUAND and A. LEULIER, J. de physiol. et de path. gén. **25**:308, 1927.

The metabolism of iron is affected in proportion to the progress of scurvy and the accompanying anemia; the administration of a diet rich in vitamin C ameliorates it in proportion to the recovery of the subject from scurvy. Although the content of cholesterol in the blood, liver, lungs and kidney remains normal in the scorbutic guinea-pig, that of the suprarenal glands is markedly diminished. Simple inanition does not affect the content of cholesterol in the suprarenal glands, but leads to a hypercholesterolemia. Metabolism of dextrose and phosphorus does not appear to be affected in scurvy.

KUGELMASS, New York.

SERUM PROTEIN. M. JACCATTET, Nourrisson **16**:341 (Nov.) 1928.

The technic of estimating the serum protein by the refractometer is described in detail, followed by a comprehensive review of the German literature. The author made observations on sixteen normal infants, obtaining an average of 7 per cent. The infants less than 6 months of age gave an average of 6.6 per cent, while those between 6 and 12 months of age showed 7.5 per cent. In two cases of dyspepsia, increases were noted due to a concentration of the blood serum (8.2 per cent). Four cases of dehydration also showed increases (7.3 per cent). Eight cases of athrepsia gave an average of 7.2 per cent. One case of pulmonary edema gave a reading of 6.2 per cent during the acute phase; with convalescence this value increased to 6.8 per cent. A case of nephrosis in an infant, aged 2 months, showed an initial reading of 3.5 per cent which decreased to 2.6 per cent before death.

MCCLELLAND, Cleveland.

THE FILTERABLE ELEMENTS OF THE TUBERCULOSIS BACILLUS AND THEIR RÔLE IN HEREDITY AND BACILLARY INFECTION. J. VALTIS, Paris méd. **2**: 37 (Jan. 12) 1929.

The author makes an excellent review of the European literature that deals with the possibility of an ultra-virus of the tubercle bacillus. A complete bibliography is given.

SANFORD, Chicago.

STUDIES OF THE BLOOD OF WHITE RATS IN EXPERIMENTAL RICKETS. E. WOENCKHAUS, Arch. f. exper. Path. u. Pharmakol. **122**:44, 1927.

A reduction in blood pigments and in the number of red cells is associated with the use of diets poor in phosphorus and in vitamin A. In white rats, the number of mononuclear and transitional cells is greatly increased and myelocytes frequently appear. With the red cell picture, changes occur; normoblasts appear and there is polychromasia. In extreme cases, nuclear degeneration becomes evident. The addition of lipoids to the diet does not completely prevent these changes in the blood picture, although the characteristic skeletal changes may be prevented. In rickets the blood changes antedate obvious changes in the skeletal system.

THE RELATION BETWEEN THE ANTIRACHITIC ACTIVITY AND THE DIELECTRIC CONSTANT OF CHOLESTEROL SOLUTIONS IRRADIATED WITH ULTRAVIOLET LIGHT. PHILIPP ELLINGER, Arch. f. exper. Path. u. Pharmakol. **122**:238, 1927.

Oils and solutions of cholesterol in alcohol and paraffin exposed to ultraviolet light show an increased dielectric constant. This change does not occur in the absence of oxygen, while the antirachitic effect of irradiation is independent of the presence or absence of oxygen. The increased dielectric constant apparently is due to the formation of products of oxidation in the cholesterol.

MINERAL METABOLISM DURING THE ADMINISTRATION OF CALCIUM. W. KRANE, Arch. f. d. ges. Physiol. **217**:24, 1927.

To maintain a calcium equilibrium, from 1.2 to 1.5 Gm. of calcium must be ingested each day. The calcium chloride of the food is absorbed in considerable amount. The administration of calcium is without influence on the nitrogen metabolism, although in the experimental administration of calcium the excretion of nitrogen in the feces is diminished. Calcium retention is accompanied by a retention of phosphorus oxide. With diets poor in calcium and sodium chloride, the body loses calcium, but if calcium chloride is given the loss is diminished. With a retention of calcium there is a loss in chlorine, and also of potassium and sodium. The addition of calcium to a diet poor in calcium and sodium chloride causes a loss in potassium, although the previously existing disturbance in sodium is obviated.

ALIMENTARY DYSTROPHY. E. ABDERHALDEN, Arch. f. d. ges. Physiol. **217**:88, 1927.

Pigeons fed on polished rice may be maintained in good condition for as long as a month, although the function of the sex glands may be somewhat disturbed, if only 0.1 Gm. of dry yeast is given. With 0.2 Gm. they may be kept in good condition for a longer time. The addition of sodium chloride to the diet of rice causes an abrupt fall in body weight; diiodotyrosine causes a similar action. When the pigeons are fed exclusively on meat for a period of five months, marked changes take place in the integument, involving particularly the feathers.

BUFFER CAPACITY AND PLANT JUICES. FRANZ LEUTHARDT, Kolloidchem. Beihefte **25**:1, 1927.

Titration curves for expressed sap are compared with titration curves for pure solutions of constituents of the plant juices. Certain nonelectrolytes, such as glycerol, sucrose and alcohol, which may increase the ionization of acids, are regarded as negative buffers. Formulas are devised which permit the determination of the distribution of the bases in the individual acids in a mixture of different polybasic acids with their salts. Titration curves for the juice from a number of fruits and succulent plants indicate that the buffering capacity may be attributed almost entirely to organic acids. Dextrose and sucrose increase the H-ion concentration of solutions of malic and tartaric acids, while they act as buffers in solutions with an alkaline reaction. The significance of organic acids in nutrition and especially their origin from carbohydrates or higher fatty acids are discussed.

KUGELMASS, New York.

PHOSPHATE LYSIS BY THE ESTERS OF RED BLOOD CORPUSCLES. OTTO JÄGER, Ztschr. f. Kinderh. **46**:159 (July) 1928.

It is known that artificial hexose monophosphate salts are split by human serum into carbohydrate and phosphoric acid, an effect probably due to phosphate esters. In an attempt made by Jäger to study such esters in red blood corpuscles, he found that phosphate lysis occurs in vitro under the same experimental conditions in infants with rickets as in healthy infants and in adults.

THE PHYSIOLOGY OF DIGESTION IN INFANTS: III. THE RÔLE OF BILE IN THE DIGESTION OF PROTEIN. E. FREUDENBERG, Ztschr. f. Kinderh. **46**:164 (July) 1928.

By titration in an alcoholic solution according to the method used by Willstätter, it was demonstrated that, if conditions were optimal, bile assisted the tryptic lysis of protein with an acid reaction. Similarly, as Freudenberg showed earlier for the lipase of human milk, bile emancipates a part of the breakdown of protein from the optimum reaction. Only the formation of high molecular products is helped, not that of the amino-acids. The combined activity of bile and tryptase quickly causes retrogression of the precipitation by rennin, and likewise coagulation by acid; here, also, is a favorable influence of bile on the digestion of protein. The point of application of bile lies apparently in the substrate, not in the ferment.

THE PHYSIOLOGY OF DIGESTION IN INFANTS: IV. A NEW CONTRIBUTION TO THE DIGESTION OF FAT. E. FREUDENBERG, Ztschr. f. Kinderh. **46**:170 (July) 1928.

The prolipase of human milk adheres to the globulin but can be separated thoroughly, purified and then activated according to a method described in an earlier article. Soluble calcium salts strongly increase the activity of human milk lipase activated by bile. On the other hand, in the beginning these salts slow human milk lipase activated by lipokinase; in the later phases of cleavage, they assist it strongly. Sodium soap has a decidedly retarding action on the lipase of human milk. If one of the activating bile salts or lipokinase continues to work after the other has ceased, the increase obtained is small unless inactivated proferment is left. Lipokinase is injured in watery solution by acid, and indeed its value under p_H 3 is irreversible. This condition shows that a breast-fed infant has the choice of digesting either fat or protein in the stomach but that it cannot complete both tasks at the same time. The young breast-fed infant, for the most part, digests fat in the stomach, and the older child, albumin. Lipokinase joins the glycerin extract of the mucous membrane of the stomach but does not appear to be obtainable in the stomach of animals other than the dog and cat. It is more stable in glycerin than in water. Lipokinase is not demonstrable in all parts of the intestine. It appears to be an agent for the digestion of fat in the stomach of the breast-fed infant; it is specific for place but not for age or kind.

THE PHYSIOLOGY OF DIGESTION IN INFANTS: V. THE ACTIVITY OF KILLED COLON BACILLI IN THE WORK OF THE INTESTINAL FERMENTS. HANS LIEPMANN, Ztschr. f. Kinderh. **46**:184 (July) 1928.

Experiments were conducted in vitro to discover whether the bodies of killed bacteria possessed the power of preventing by adsorption the activity of the ferments of digestion. All quantitative researches made on intestinal lactose, intestinal saccharose, pancreatic amylase and human milk lipase answered the question negatively.

THE PHYSIOLOGY OF DIGESTION IN INFANTS: VI. THE INFLUENCE ON EREPSIN AND TRYPSIN OF THE FERMENTATIVE ACTION OF COLON BACILLI. O. BUDDE, Ztschr. f. Kinderh. **46**:195 (July) 1928.

It is possible to study the influence of the fermentative and putrefactive products of bacilli which can be found in the endogenous invasion of the upper regions of the duodenum by bacteria; the influence of colon bacilli on erepsin and trypsin can likewise be determined. The action of intestinal erepsin is showed by butyric acid, capronic acid, acetic acid and lactic acid and, by the exclusion of acid activity, permits the demonstration of a distinct anion activity. Formic acid, succinic acid and the amines formed from peptones are without activity. The peptone bodies themselves slow the action of erepsin. The bodies of colon bacilli, in the living and killed state, slow the action of erepsin in the majority of cases. None of the tested substances influence trypsin in its activity.

THE PHYSIOLOGY OF DIGESTION IN INFANTS: VII. THE ELIMINATION OF TRYPTASE AND PEPTIDASE IN THE STOOL OF THE INFANT. O. BUDDE, Ztschr. f. Kinderh. **46**:202 (July) 1928.

The quantity of tryptase and peptidase eliminated in a twenty-four hour stool of infants fed on the breast and on the bottle was determined by Budde. In breast-fed children the value of tryptase per unit of weight of stool lies definitely lower than that of peptidase, especially in comparison with infants fed on the bottle. The small content of peptidase in the stool after ingestion of human milk is related to the injury of ferments by fermentative acids. The daily quantity of ferment eliminated depended on the amount of the stool.

THE PHYSIOLOGY OF DIGESTION IN INFANTS: VIII. DIGESTION IN THE STOMACH. ELISABETH SCHEMANN, Ztschr. f. Kinderh. **46**:210 (July) 1928.

Complete precipitation of human milk is reached between p_H 5.8 and 5.0. The optimum lies at p_H 5.4 to 5.0. At first, lipolysis slows the precipitation by rennin, but later in digestion it aids indirectly in the forming of the acidity into a more favorable zone of reaction. The buffer value of lipolyzed human milk is definitely higher than that of unchanged breast milk. On this fact is based a titrometric method which gives the grade of lipolysis. In the young healthy infant fed during the first three months on pure human milk or on cow's milk diluted two-thirds, the acidity of the contents of the stomach is conditioned mostly by lipolysis and only rarely by the secretion of hydrochloric acid. By a consideration of the dilution of human milk ingested, the buffer value is found to be from three to six times as high as that of unchanged human milk. In the older child, fed on solid food, lipolysis plays no part after the ingestion of human milk. If the dilution is considerable, the buffer value is hardly different from that of unchanged human milk. The secretion of hydrochloric acid and the quantity of gastric juice do not run parallel in the young infant. The work of Rosenbaum-Hoffman on the small quantity of secretion in natural feeding is confirmed, but when older children fed on solid food are given breast milk there is often a stronger diluting secretion in the stomach. In dyspeptic disturbances a diminished lipolysis occurs in some cases.

INSENSIBLE PERSPIRATION IN THE INFANT: II. ITS DEPENDENCE ON THE CALORIC INTAKE. DE RUDDER, Ztschr. f. Kinderh. **46**:384 (Sept.) 1928.

Perspiration in the infant appears to be a function of two variables, fluid intake and energy intake. Every increase of these two factors leads to an increase of perspiration but that caused by an increase in the energy intake is unequivocally dependent on the water at hand; that is, the water added. When an intake of water is more than 700 cc., an increase of energy of 100 per cent causes an increase of perspiration of about 100 per cent. With a diminished fluid intake, the effect of the increase in energy is increasingly less. The last established fact is in good agreement with the theory of the stagnation of perspiration in infants fed on concentrated and rich food.

EMERSON, Boston.

A STUDY OF CALCIUM AND INORGANIC PHOSPHORUS IN THE SERUM OF RABBITS WITH EXPERIMENTALLY PRODUCED RICKETS. AKI OHNO, J. Pediat. (Tokyo), December 20, 1928, no. 343, p. 2055.

The first part of the author's experiments was to determine the amount of blood calcium and phosphorus in normal rabbits, which she found to be variable according to the stage of growth and also in relation to the intake of food. As to the quantity of blood calcium, the author found that the younger the rabbit the greater the value, whereas the amount of inorganic phosphorus seemed to increase with age. The value of calcium is also greater a few hours after adequate feeding than at the time of starvation. On the whole, however, the average value of calcium for normal rabbits was 11.8 mg. per hundred cubic centimeters, and the

phosphorus was 7.5 mg. per hundred centimeters, giving a calcium-phosphorus ration of 1 : 5. In contrast with the fairly uniform values for both calcium and inorganic phosphorus in normal rabbits, the author obtained a great variation in both in rabbits which were experimentally rendered rachitic. The lowest calcium value was 7.1 mg. per hundred cubic centimeters, while the highest was 14.8 mg. per hundred cubic centimeters, the average being 13 mg. The lowest phosphorus value was 3.2 mg. per hundred cubic centimeters, and the highest 10 mg., the average being 8.6 mg. These last figures, however, give the same calcium-phosphorus ratio of 1 : 5. The author concludes that outside of great variations in the quantities of calcium and inorganic phosphorus in rachitic rabbits, as compared with fairly constant values in normal animals, no definite proof of either the increase or the decrease may be demonstrated.

KATO, Los Angeles.

Nutrition

OTOLOGIC AND OTHER MANIFESTATIONS OF A DIET DEFICIENT IN VITAMINS; ANIMAL EXPERIMENTATION. ROY A. BARLOW, Arch. Otolaryng. **8**:629 (Dec.) 1928.

Various investigations in the field of vitamins are discussed, and from these and the work carried on by the author he concludes that, as neither bone nor nerve tissue can be demonstrated to be affected by diet deficient in vitamin A or B, such deficiency cannot be held responsible for deafness. Since a lack of vitamin A, however, causes changes in the mucosae of the respiratory tract, it is possible to believe that it may thus produce chronic changes in the soft tissues of the ear, which may interfere permanently with hearing. Further study of vitamins in their relations to minerals and the metal salts of bones may eventually be of great value in the knowledge of the content of bone.

BARNETT, Chicago.

DISTURBANCES OF GROWTH. CLYDE MOORE, M. Clin. N. Amer. **12**:433 (Sept.) 1928.

The growth of an organism is dependent on two main factors: the substances taken into the body, and the mechanism through which these substances are utilized. The latter include such diverse elements as the chemistry of metabolism, light, the functioning of the glands of internal secretion, intercurrent disease and heredity. Three cases of disturbance of growth are reported in which some hormonic dysfunction was an important factor. Two patients with pituitary deficiency associated with diabetes insipidus were treated with pituitary and thyroid extract and showed definite improvement. In one case of Herter's intestinal infantilism, after slow improvement under dietary treatment, there was sudden and remarkable progress following an attack of chickenpox. The author suggests that the improvement in this case may have been the result of the activation of certain of the glands of internal secretion by the infective process.

THE UNDERNOURISHED CHILD. H. B. HAMILTON, M. Clin. N. Am. **12**:489 (Sept.) 1928.

The so-called standards of weight, height and age are of value, but they do not necessarily reflect the true index of a child's nutritive condition. Much propaganda put out by various organizations by means of newspapers, magazines and untrained or semitrained persons is misguiding and harmful.

Infections must be eradicated if undernutrition is to be successfully managed. Not infrequently the overconsumption of milk is a disturbing factor in the child who is otherwise well but under-weight. Nothing short of a careful history and a thorough physical examination can form an adequate basis for intelligent treatment. This cannot be done wholesale. Endurance, the ability to undergo physical or mental activity without illness, and peevishness or excessive fatigue, form a better criterion of fitness than the mere relation of age, height and weight.

SMITH, Ogden, Utah.

A Brief History of Rickets Therapy. T. Swann Harding, M. J. & Rec. **129**:16 (Jan. 2) 1929.

The author gives in an interesting way the history of the therapy for rickets from 1807 to the present day. He states that in 1807 Bardley spoke of using cod liver oil effectively for women worn out by "rheumatism" after pregnancy. These attacks, he says, were almost certainly due to a depletion of calcium in the bones. He shows that cod liver oil came into vogue as a therapeutic agent for rickets and went out of fashion several times before the present day.

In 1845, the remedial measures included a purge with mild mercurous chloride twice a week, a diet composed mostly of starches, and a liberal dosage of iron, quinine and port wine. In the eighties, some physicians asserted that starch caused rickets and removed starch from the diet of children. In 1897, certain German authors claimed that persons with rickets could be cured by phosphorus but added that better results were secured if the phosphorus was added to cod liver oil. In 1899, it was claimed that rickets was caused by faulty diet and that it was the result of taking milk out of the diet too early. In 1908, it was asserted by Ebball that rickets was caused by lack of light and that patients with it could be cured by exposure to the sun's rays. In the same year, Findlay claimed that they could be cured by proper exercise. In 1912, pituitary gland extract was used, but it was stated that better results were secured by the addition of calcium.

In 1914, Salge suggested that vitamins would cure persons with rickets. Ultraviolet rays from a carbon arc lamp were used in the treatment for rickets in 1922 by Hess and Unger. The use of activated ergosterol as a cure for the disease was reported by Hess and Lewis in 1928.

Feeding the Baby. Alexander Nettelroth, M. J. & Rec. **128**:277 (Sept. 19) 1928.

Mother's milk and cow's milk, however modified, are not complete foods, both being deficient in vitamins. These inadequacies should be supplied from birth. When the infant is 3 months old or earlier, the author advises the addition of three meals a day, comprising finely chopped meats, the juice of vegetables and thinned cereals. In cases of anaphylaxis to milk, the milk should be abolished and replaced by broth, the juice of fruits and vegetables, cereals and finally by chopped meat.

He said that no digestive disturbance will follow the change to a well balanced diet other than milk if the accessory food factors are included; the molecular structure need not closely resemble mother's milk; it may vary from it greatly and surpass it in digestibility and growth-promoting properties.

Williamson, New Orleans.

Comparison of the Utilization of Nucleic Acids of Animal and Vegetable Origin. T. Brailsford Robertson, C. Stanton Hicks and H. R. Marston, Australian J. Exper. Biol. & M. Sc. **4**:125, 1927.

Nucleic acids from ox spleen and yeast were fed to the same human subjects subsisting on an otherwise purine-free diet. Animal nucleic acid is absorbed from the alimentary canal slightly less well than vegetable nucleic acid. The output of uric acid is much greater after the ingestion of vegetable nucleic acid than after animal nucleic acid. The daily dose of 15 Gm. eaten in these experiments led to a deficiency in the function of the kidneys. This loss of renal activity induced retention of the various metabolites to the extent of vitiating comparisons of output when the two types of nucleic acid were successively administered. Only with uric acid was the excess of production with vegetable nucleic acid sufficient to overcome the retention attributable to a previous administration of nucleic acid of animal origin.

Acid of either origin administered by mouth leads to the appearance of one or more substances other than creatinine which react with impure picric acid in alkaline solution, but do not react with picric acid which has been purified by

recrystallization from benzene. No leukocytosis or alteration of the differential white cell count is induced by oral administration of either form of nucleic acid. The fact that yeast induces leukocytosis is therefore not attributable to its content of nucleic acid. On an equal intake of nitrogen, meat is preferable to vegetables if it is desired to reduce the production of uric acid from the diet.

KUGELMASS, New York.

VITAMINS A AND D OF SPINACH. S. G. WILLIMOTT and FRANK WOKES, Biochem. J. **21**:887, 1927.

Daily doses of 25 mg. of an acetone-ether extract of dried spring spinach prevented xerophthalmia and induced satisfactory growth in rats. The extract does not appear to contain significant amounts of vitamin D.

IRRADIATED MILK: ITS EFFECT ON THE BLOOD. VERONICA DAWKINS and C. LEE PATTISON, Lancet **2**:1314, 1926.

Milk exposed daily to the rays from a mercury vapor quartz lamp at a distance of about 2 feet for one-half hour caused an increase in the number of erythrocytes in five patients with an original low red cell count. Milk which had not been irradiated was then given to these patients and caused a decrease which was again followed by an increase if irradiated milk was given. The amount of hemoglobin varied.

KUGELMASS, New York.

NOTES ON ACUTE ACIDAEMIA IN CHILDHOOD. JULES REY, Practitioner **121**:260 (Oct.) 1928.

Acute acidemia is a purely chemical condition due to faulty feeding and is a rarity in breast-fed infants. When carbohydrates are added to the food, at the age of 8 or 9 months, it is a great mistake to add any cooked protein. The diet of milk and carbohydrates should be continued until the child is 2 or 3 years of age, pasteurized milk and raw albumin water being the only protein form of food given. Animal fats should be avoided also. After the child is 2 or 3 years of age, lightly boiled egg, meat gravy and steamed fish may be added carefully, the child being watched all the time for symptoms of acidemia.

The symptoms of acidemia are well marked. The prodromal symptoms are increased appetite followed by loss of appetite, then malaise, headache, vomiting and, finally, unconsciousness and death. Acetone breath and acetone and diacetic acid in the urine follow the vomiting.

After the age of 8 years, the possibility of the child developing acidemia tends to disappear. The assimilative power in respect to protein is much advanced in the sexually precocious child; the converse obtains in the hypogonads.

The treatment is the administration of large amounts of alkalis with or without insulin. After an attack, sodium citrate should be given for several months. Prophylaxis is important, and diet is all important.

Ultraviolet rays and irradiated autoserum therapy are of advantage.

RUMINATION IN INFANTS. DONALD PATERSON, Practitioner **121**:726 (Dec.) 1928.

Rumination in infants is not infrequently found as a cause of failure to gain. The condition usually occurs in infants between the ages of 3 and 7 months, the majority are girls.

The mother seldom complains that her child is vomiting badly, but notices that the child's pillow is always wet. The child refuses to ruminate in front of the mother, physician or nurse, so the process must be watched at the head of the bed or through a screen.

Immediately after a feeding, the infant will be seen to strain and arch its back. The food wells up into the mouth, gulping movements are made and the milk is spilt from the corners of the mouth.

Roentgen and postmortem examinations show no organic disease present. The complaint is purely a functional one.

Among the many methods of treatment that have been suggested are: dropping a solution of quinine into the open mouth of the ruminating infant (from some facetious American observers); plugging the nostrils with cotton wool, and placing a skull cap on the head with strings which tie tightly beneath the chin.

No method, however, compares with the use of the thick feeding. It is more difficult to vomit a thick feeding; even if some food is vomited, the increased caloric value of the portion retained will make the child thrive.

An occasional gastric lavage is often a great help.

PAUL S. BARRETT, San Francisco.

DYSPEPSIA IN CHILDHOOD. JULES TAILLEUS, Proc. Roy. Soc. Med. **22**:127, 1928.

1. A child with dyspepsia rarely, and an infant never, complains of indigestion. It is only from the age of 10 years that subjective symptoms exist. It follows, therefore, that dyspepsia in childhood is often hidden and has to be searched for in order to be diagnosed.

2. Dyspepsia in children often takes a misleading form, as it produces a general weakness and wasting, often slight fever, and even coughing. It is therefore frequently confused with tuberculosis.

3. Dyspepsia in children is a functional complaint. Its cure is therefore almost invariably easy and often rapid.

4. The different digestive actions depend on one another. It is usually the first which causes dyspepsia in children. In other words, such dyspepsia originates in the stomach.

5. In more than three fourths of these children, the gastric trouble consists of hyperchloracidity.

6. Treatment is as follows: an approved diet, which chiefly consists of milk and farinaceous foods, a two hours' rest after meals, and the administration of alkalis. A quick progress toward a complete cure is observed; there is a particularly rapid increase in weight. Statistics drawn up from 200 cases show this, and also that such hyperchloracidity can reach high figures even in very young children.

AUTHOR'S SUMMARY.

THE FEEDING OF CHILDREN WITH ECZEMA. L. RIBADEAU-DUMAS and M. LEVY, Bull. Soc. de pédiat de Paris **8**:427 (Oct.) 1928.

The authors present a case of long standing eczema in an infant, aged 13 months, with moderately low serum protein (5.6 per cent) and bad general nutrition. All milk except yoghourt was omitted from the diet; later, 80 Gm. of raw veal liver and 800 cc. of milk were given. The nutrition improved as did the eczema. The author refers to Epstein (*Jahrb. f. Kinderh.*, 1929, p. 117).

CLAUSEN, Rochester, N. Y.

INFLUENCE OF VEGETABLES ON THE GASTRIC SECRETION. J. H. KELLOGG and V. N. BOLDUIREV, Compt. rend. Soc. de biol. **95**:1145, 1926.

Experiments with dogs proved that fresh vegetables excite a secretion of the gastric juice which is as rapid, abundant, prolonged and high in pepsin content as gastric juice stimulated by meat extracts. Raw or cooked vegetables and juice of fruits cause a less abundant flow of gastric juice than do vegetable or meat extracts. The extracts of cereals are much less marked in their stimulating action on the gastric juice than are the extracts of other vegetables.

KUGELMASS, New York.

COLLOID CHEMISTRY APPLIED TO THE PROBLEM AND TECHNIC OF ARTIFICIAL FEEDING OF INFANTS. G. C. BENTIVOGLIO, Riv. di clin. pediat. **26**:889, 1928.

The author has added gum arabic (from 1.5 to 6 per cent) to cow's milk. During digestion, it acts as a colloid protector, the casein of the milk being precipitated in smaller and softer particles. The author presents the reports of five cases in which this feeding was used. The digestion was better, the bowels were more regular and the stools more homogeneous. The infants, several of whom presented nutritional problems, showed clinical improvement.

HIGGINS, Boston.

THE INFLUENCE OF THE FEEDING OF BONES ON THE SECRETION OF INTESTINAL JUICE AND ITS COMPOSITION. I. V. BOLDUIREV, Fermentforsch. **9**:146, 1927.

The amount of succus entericus secreted in a given time outside of the period of digestion is greater than that secreted during the period of digestion. The secretion is always periodic, both during and outside of digestion. The periods of secretion recur two or three times oftener outside than within the periods of digestion. To perform the experiments in a physiologically correct manner, one should not treat the mucosa with any artificial stimulant. The feeding of bones increases the amount of secreted juice as well as its alkalinity, mineral and mucous content, and promotes the metabolism and peristalsis of the dog. It is especially important that no accidental external irritation of the isolated intestine occurs during the experiments or in the time intervening. In performing the operation for the purpose of isolating the intestinal loop, two precautions must be observed: The loop should not be longer than 25 or 30 cm., and it should be fastened to the spinal column in such a manner that the juice can flow out rapidly; otherwise, the juice can be easily absorbed by the intestinal loop. Bacterial infection, such as diarrhea or abscess in the region of the fistula, can bring about an excessive secretion. In such cases, the juice is relatively dilute.

KUGELMASS, New York.

PHYSIOLOGIC CRANIOTABES? I. ROSENSTERN and G. BRUNS, Ztschr. f. Kinderh. **46**:270 (July) 1928.

In craniotabes in the young infant, especially during the beginning of the disturbance, one often finds normal serum phosphate values and a normal x-ray picture, observations which are often taken as evidence for the existence of a physiologic craniotabes. That such a conclusion is not correct is shown by the report of a series of clinical, roentgenologic and blood chemical researches in young infants with craniotabes.

THE ABSORPTION AND RETENTION OF HEN EGGS (NITROGEN, PHOSPHORUS, SULPHUR, ETC.) IN INFANTS. A. RUOTSALAINEN, Ztschr. f. Kinderh. **46**:370 (Sept.) 1928.

In feeding hen eggs to infants, a positive balance is reached in relation to substances containing nitrogen and fat and mineral substances, especially phosphorus and sulphur. Hen eggs, therefore, may be used to advantage, especially in the nourishment of rachitic children.

THE QUESTION OF THE INFLUENCE OF IRRADIATION ON THE FORMATION OF MILK IN THE NURSING MOTHER. W. FREUND, Ztschr. f. Kinderh. **46**:429 (Sept.) 1928.

Lactagogues can be studied exactly in their activity only in cases of genuine hypogalacty, not in the bringing back of transiently diminished secretion of milk because here no quantitative determination is possible. Irradiation of the breast with the sun's rays is without influence in true hypogalacty. It is not impossible that under the proper conditions, a transiently diminished secretion of milk may be favorably influenced, possibly by suggestion, an action which is recognized in other lactagogues.

EMERSON, Boston.

Prenatal Conditions

THE PRESENT STATUS OF OUR KNOWLEDGE OF THE EFFECT OF IRRADIATION UPON THE GENERATIVE ORGANS AND THE OFFSPRING. HALSEY J. BAGG, Am. J. Roentgenol. **16**:529 (Dec.) 1926.

It seems that the effects of irradiation on living tissues are mainly destructive, especially to immature and actively dividing cells. Irradiation of the unfertilized ova or spermatozoa may result in either completely destroying the functional activity of these cells or so modifying their structure that the resulting offspring may be defective, most probably through the death and absorption of the injured germ cells. Hereditary abnormalities may result through modification of the germ cells. Irradiation during early pregnancy is likely to produce a marked arrest in development, with subsequent modification of structural expression. Irradiation during later pregnancy may produce changes which will be manifested as developmental defects and loss of fertility, not observable at birth. There is at present no agreement as to the sterilization dosage for human beings.

STULIK, Chicago.

CONGENITAL ATRESIA OF BILE DUCTS. COURSEN BAXTER CONKLIN, Internat. Clin. **4**:215 (Dec.) 1928.

The differential diagnosis of five types of icterus of new-born infants is given: (1) icterus neonatorum, a benign evanescent type; (2) icterus associated with congenital obliteration of the bile ducts, which is found in 16 per cent of the cases and which is operable; (3) familial icterus, a fatal disease with a tendency to repetition in the family; (4) congenital hemolytic icterus, characterized by increased fragility of corpuscles, and associated with anemia, a high color index and a mononuclear leukocytosis; (5) icterus in association with sepsis.

The author reports a case of congenital obliteration of the bile ducts in an infant who was operated on and who lived to be nearly 14 months old.

MILLER, South Bend, Ind.

LEONTIASIS OSSEA. N. B. CAPON, Arch. Dis. Childhood **3**:285 (Dec.) 1928.

A case of the diffuse osteitic variety of leontiasis ossea is described in a boy, aged 14 years. Photographs and roentgenograms illustrate the case.

HEMIHYPERTROPHIE ALTERNE. A. D. FORDYCE, Arch. Dis. Childhood **3**:300 (Dec.) 1928.

The literature is reviewed and a case of hemihypertrophie alterne in a child, aged 4 years, is presented.

PETERMAN, Milwaukee.

THE TRANSPORT OF CALCIUM FROM MOTHER AND CHILD AND CALCIUM DEPOSITS IN THE PLACENTA. ALBERT SCHÖNIG, Ztschr. f. Geburtsh. u. Gynäk. **94**:451 (Dec.) 1928.

It has been possible, by means of the precipitation of calcium as oxalate crystals and the use of polarized light, to demonstrate calcium in the normal placenta of pregnancies of from three to six months' duration. This is regarded as transport calcium for the fetus and has nothing to do with the calcareous degeneration.

It has been shown from the morphologic picture and clinical investigation that the placenta takes up calcium through the activity of the chorionic epithelium.

The cell membrane of the chorionic epithelium corresponds to a semipermeable membrane. The transportation of the calcium from the villus stroma to the fetal blood takes place by diffusion through the fetal endothelium. By this new method it is possible to demonstrate much more calcium in degenerated portions of the placenta than was heretofore possible. The deposits of calcium in the mature placenta have in themselves no significance for the life of the fetus.

ADAIR.

FURTHER RESEARCHES ON THE REGULATION OF THE TEMPERATURE OF WEAK AND PREMATURE INFANTS. A. ECKSTEIN and H. PAFFRATH, Ztschr. f. Kinderh. **46**:305 (Sept.) 1928.

The frequency of the pulse rate of human beings, especially that of infants whether full term or premature, follows the law of van't Hoff exactly; for example, with an increase of temperature of 10 degrees, the frequency of the pulse rate is doubled. Since the reaction to the surrounding temperature is not a simple chemical reaction, it is evidence of power of good accommodation. Moreover, the frequency of respiration shows an increase, apparently as an expression of increased metabolic activity. This relation does not coincide completely with that between quickness of reaction and temperature, on account of the condition of the mechanism of breathing at this early age. The behavior of the two important automatic centers, that of the heart and that of the lungs, in varying temperatures of the body is a measure of efficiency under physiologic and pathologic conditions and should not be valued too lightly, especially in weak infants. It shows that in such a biologic breadth of reaction no immaturity exists.

EMERSON, Boston.

Diseases of the New-Born

A CASE OF ARACHNODACTYLISM IN A NEWLY BORN INFANT. G. SCHREIBER, DUHEM and JUBERT, Bull. Soc. de pédiat. de Paris **8**:397 (Oct.) 1928.

Although only about twenty cases of this disorder have been reported, the authors have observed three cases within eighteen months. The present patient, at the age of 7 weeks, presented the following features: great elongation of all extremities, relaxation of all joints, muscular atony and athrepsia. On supplementary feeding, the infant attained normal weight but developed clinical signs resembling rickets. Roentgenograms, however, showed no rachitic changes. Ossification of the carpal bones appeared more advanced than normal. The sella turcica seemed large.

TETANUS NEONATORUM WITH RECOVERY. M. H. GRENET and G. VOGT, Bull. Soc. de pédiat. de Paris **8**:407 (Oct.) 1928.

Developing the symptoms of tetanus on the twelfth day, the patient received twelve daily injections of 20 cc. of antitetanus serum partly intramuscularly and partly subcutaneously. Recovery occurred.

CLAUSEN, Rochester, N. Y.

THE PREVENTION OF OMPHALITIS. HORIA SLOBOSIANO, Nourrisson **16**:376 (Nov.) 1928.

Attention is directed to the too high infant mortality from umbilical infections, due either to the ordinary pyogenic micro-organisms or to the tetanus bacilli. The author emphasizes the fact that the 70 per cent alcohol is more bactericidal than stronger or weaker solutions and that tetanus spores can be killed by weak solutions of silver nitrate. She recommends daily dressings soaked in the following solution: silver nitrate 0.4 cc., distilled water 50 cc. and alcohol (95 per cent) 150 cc. The use of the dressings should be continued during the first month until the cicatrization of the umbilical wound and the fibrosis of the vessels are complete.

McCLELLAND, Cleveland.

THE SECRETION OF THE INFANT'S BREAST. KARL JAROSCHKA, Monatschr. f. Kinderh. **42**:523, 1929.

The author attempted to determine the time of the appearance and disappearance of colostrum bodies and their relation to secretion in the breast of infants. Of twenty-one new-born infants in only one was there secretion on the first day, although in twelve infants the breasts were quite infiltrated. Ten of these twelve showed secretion from the third to the fifth days. In only two cases were colostrum bodies found. In a series of fifty-eight children, aged from 6 to 120 days, the

secretion was studied by means of a capillary pipet, the drop then being placed on a glass slide under a cover glass. Secretion occurs only rarely after the hundredth day. It usually stops between the ages of 30 and 100 days. In four underweight, breast-fed children, only fat droplets with no colostrum bodies were found. Probably the quantity of colostrum bodies depends on the amount of fat in the secretion. In 28 per cent of the infants, the colostrum corpuscles reached their greatest number between the twelfth and fortieth day, while in the remainder they seemed to increase steadily until the termination of the secretion. In six cases there was a decided decrease so that at the end of the experiment the corpuscles had dropped from 638 to 5.

GERSTLEY, Chicago.

Acute Infections

OBSERVATION ON CERTAIN ETIOLOGICAL FACTORS IN RHEUMATISM. LERCY PORTER SUTTON, Am. Heart J. **55**:145 (Dec.) 1928.

In an analysis of about 1,000 cases of heart disease in children in the Bellevue Hospital and general pediatric clinic, those from certain countries, including the Italian, Irish and native American, were found to be more susceptible to rheumatism than others, such as Spanish, Armenian and Jewish. Girls were affected slightly more frequently than boys; the average age of most patients was determined to be 9 years. Twenty-one per cent of the girls and 14 per cent of the boys gave no history of rheumatic infection before the discovery of involvement of the heart. A definite seasonal variation was found, with the greater incidence in the spring months.

MANNING, Santa Barbara, Calif.

CERTAIN ASPECTS OF IMMUNIZATION IN COMMUNICABLE DISEASES OF CHILDHOOD. JAMES M. ANDERS, Internat. Clin. **4**:165 (Dec.) 1928.

Anders presents a review of the historical development and practical application together with detailed methods of immunization in smallpox, diphtheria, scarlet fever, measles, chickenpox and pertussis.

MILLER, South Bend, Ind.

PREDISPOSING FACTORS IN RHEUMATIC INFECTION IN CHILDHOOD. A. DINGWALL FORDYCE, M. J. & Rec. **128**:460 (Nov. 7) 1928.

The predisposing factors in rheumatic infection in childhood are: (1) an unstable nervous system, (2) digestive disorders and (3) weakness of the lymphoid defense. The first two factors are usually closely associated, yet the third may result in rheumatic infection without either of the first two conditions being pronounced. When all three factors are marked, there is serious danger of infection of the heart and of chorea. When the first two alone are marked, chorea is more likely to occur. When lymphoid weakness alone is pronounced, the danger is of infection of the heart and there is little fear of chorea. These predisposing factors are simple but, for this very reason, difficult to control. The moral seems to be that there is no royal road to the prevention of rheumatism. There is, however, a great incentive to increased activity in investigating the problem. The author feels that if there were more beds in country hospitals and suitable residential schools, the scourge of rheumatic infection of the heart would be almost completely swept from the country.

WILLIAMSON, New Orleans.

MORTALITY OF THE CURRENT INFLUENZA EPIDEMIC. Pub. Health Rep. **44**:117 (Jan. 18) 1929.

Any doubt as to the reality of the current influenza epidemic is promptly dispelled by an examination of the mortality statistics. According to the following conservative estimate, there have been, to Jan. 5, 1929, no less than 26,000 deaths in the United States attributable to the epidemic.

SANFORD, Chicago.

DIPHTHERIA: THE PRESENT POSITION. GUY W. J. BOUSFIELD, Practitioner **121**:237 (Oct.) 1928.

A review of the present situation in regard to the control of diphtheria reveals an eminently unsatisfactory condition.

In one borough of London, one death among ten children was caused by diphtheria.

Many would express surprise to find a patient unprotected against smallpox; yet the following facts appear in a comparison of the two diseases: Smallpox is rare and now seldom fatal. Diphtheria is common and often fatal. The modern methods of immunizing against diphtheria are just as efficient and rather more precise than those employed in the control of smallpox.

One of the greatest difficulties in the treatment for diphtheria is the early differential diagnosis. A definite diagnosis is often made with difficulty. If a swab is taken and the result of bacteriologic culture is waited for, a fatal delay often occurs before treatment is begun.

Rational treatment demands the prompt administration of antitoxin in any case in which the diagnosis is doubtful, as the result of the bacteriologic examination may be misleading. One more potent factor is that the patient is not seen until the disease is firmly established.

Diphtheria cannot be fought on these lines. Prophylactic immunization is the only answer to the problem and, to be effective, it must be carried out by wholesale methods.

Fatal diphtheria need not exist today. The profession must make the public realize this. If the population creates the demand, public bodies will supply the facilities.

BARRETT, San Francisco.

THE INTENSIVE METHOD OF SERUM TREATMENT OF DIPHTHERIA. H. STANLEY BANKS, Proc. Roy. Soc. Med. **21**:1849 (Oct.) 1928.

The important clinical features of the type of case in which the intensive method of serum treatment was used were as follows: (1) extensive diphtheritic membrane—an ill defined glassy membrane toward the spreading margin, which was of grave import, as was also edema of the fauces; (2) cervical adenitis and periglandular edema; (3) nasal discharge, especially if hemorrhagic; a membrane in the nares; (4) a fetid odor from the throat, typical of severe diphtheria, and (5) severe toxemia characterized by delirium and restlessness or by great lethargy, and evidenced in some cases by submucous hemorrhages.

The average dose of antitoxin employed in the foregoing type of case was 70,000 units intravenously and 30,000 units intramuscularly. As much as 250,000 units was given in one case. As far as possible the whole dose was given at one time, but if after twelve or twenty-four hours the patient's response was not sufficiently good, a similar large dose was administered. The criteria of adequate dosage were the disappearance of toxic symptoms within twenty-four hours, and an opaque appearance of the membrane and the well defined edges within the same period. The death rate for the hospital was reduced from an average of 9.3 per cent over the previous decennium to 2.6 per cent during the twelve months' period under review.

WILLIAMSON, New Orleans.

DENGUE FEVER AMONG CHILDREN DURING THE EPIDEMIC AT ATHENS, 1927-1928. VERAS, Arch. de méd. d. enf. **32**:5, 1929.

Dengue fever attacked nine tenths of the population of Athens in the last epidemic. As chief of the medical service at the Polyclinic, Veras had an unusual opportunity to observe its natural history among infants and children. He discusses at length the epidemiology of dengue and the various organisms under consideration in the study of its etiology. The postnatal period seems to confer no immunity against dengue, as shown, for example, in measles, but in Athens no observations were made of immunity derived from mothers who had had the disease. Infants,

aged 5 days, and a great many others less than 3 months of age were treated. The onset of the disease was invariably brusque. There was a high temperature, often accompanied by convulsions, which, of course, is a common characteristic of many acute infections. In dengue, however, there is a remission in the temperature on about the third day, followed in from twelve to twenty-four hours by a second elevation which commonly lasts until the sixth or seventh day. The initial rash, as in adults, is not constant; Veras observed it in about one third of his cases. The eruption itself is polymorphic. There is a scarlatiniform base over which minute papules are scattered. These appear on the face, chest and abdomen on about the third day and disappear anywhere from a few hours to several days. A furfuraceous desquamation may follow the exanthem. The acute pain characteristic of invasions in adults does not seem so accentuated in infants, older children complain of a headache and aching joints. Gastric symptoms are common. The tongue is coated and the breath foul; epistaxis may be noted. Examination of the blood does not always reveal the striking leukopenia so characteristic of dengue. Relapses are uncommon. Among the complications one may find enterocolitis, nephritis and arthralgia. Treatment for the infection is entirely symptomatic.

AMESSE, Denver.

CEREBROSPINAL MENINGITIS AND OTITIS. A. MORQUIO, Bull. Soc. de pédiat. de Paris **8**:391 (Oct.) 1928.

Morquio reports four cases of meningococcus meningitis occurring in children who had had suppurative otitis media, and in whom the meningitis was at first thought to be otogenic.

MENINGOCOCCUS MENINGITIS; MENINGEAL BLOCKAGE: RECOVERY AFTER INTENSIVE SEROTHERAPY AND TREPHINING. JEAN HUTINEL, G. BOULANGER PILET and M. FÈVRE, Bull. Soc. de pédiat. de Paris **8**:394 (Oct.) 1928.

A girl, aged 6 years, in the course of meningococcus meningitis, developed a blockage. Spinal taps yielded no fluid, and the symptoms increased. Serum was given into the muscles. Following trephining, serum was injected into the ventricles, and complete recovery apparently resulted.

DYSENTERIFORM DIARRHEAS IN MEASLES. G. L. HALLEZ, Bull. Soc. de pédiat. de Paris **8**:417 (Oct.) 1928.

This is a report of two cases. In one, dysentery was eliminated by culture. In the discussion M. H. Barbier and M. Lesne offer evidence that such diarrheas are nevertheless probably due to dysentery bacilli.

HEMORRHAGIC SYNDROME IN THE COURSE OF TYPHOID FEVER: STREPTOCOCCEMIA WITH RECOVERY. J. HALLE and Y. BUREAU, Bull. Soc. de pédiat. de Paris **8**:431 (Oct.) 1928.

The hemorrhagic manifestations included blood in the stools, bleeding gums, peculiar angiomatous tumors of the tongue and hemorrhages into the conjunctivae, but few into the skin. The bleeding time was eighteen minutes and the coagulation time was normal.

CLAUSEN, Rochester, N. Y.

THE IMMUNIZING VALUE OF THE SCHICK TEST. A. PISANO, Riv. di clin. pediat. **26**:899, 1928.

The percentage of positive Schick reactions among 111 well children in Cagliari was 18 per cent. Among 53 sick children at the clinic, 32 per cent gave positive reactions.

Four repetitions of the test were made at intervals of fifteen days in twenty well children and in thirteen sick children; one of the well children and five of the sick children developed negative Schick reactions.

The author concludes (1) that repetition of the test does not itself produce appreciable immunity, and (2) that children may frequently lose their antitoxic protection temporarily as the result of an acute illness. HIGGINS, Boston.

ACUTE ENCEPHALITIS FOLLOWING MEASLES. FLORENCIO BAZÁN, Arch. latino-am. de pediat. **22**:469, 1928.

The case concerns an infant, aged 5 years, in excellent health and of good antecedents who suddenly developed recurrent convulsions following an attack of measles. The convulsions were limited to the right side. During the attacks, the child had high fever and complete coma. After cessation of the attacks, the child presented complete right-sided hemiplegia and aphasia. There was rapid improvement and, after two months, complete recovery from the condition.

In the author's opinion, the condition was due to acute encephalitis accompanied by epileptiform convulsions. SCHLUTZ, Minneapolis.

ENCEPHALITIS FOLLOWING VACCINATION. E. WALENTA, Monatschr. f. Kinderh. **42**:530, 1929.

Encephalitis developed ten days after vaccination and ran a typical course, with fever, unconsciousness and paralysis. The condition was present for three weeks, and it terminated in complete recovery. GERSTLEY, Chicago.

THE DIAGNOSTIC VALUE OF THE SKIN CHANGES IN PARATYPHOID FEVER IN CHILDREN. O. JÄGER, Ztschr. f. Kinderh. **46**:229 (July) 1928.

Of the four cases described, the first corresponded to the abdominal form of paratyphoid fever (Schottmüller), but only the changes in the skin were noteworthy. In both infants in the second and third cases, and in the fourth case, the bacteremia with fever and a widespread eruption of rose spots awoke suspicion of paratyphoid fever. From these observations it may be deduced, in harmony with the literature, that cases of paratyphoid fever, like typhoid fever in children and especially in infants, may be abortive and that the appearance of the skin is not only especially noticeable but may be the sole characteristic symptom of great diagnostic significance. The cause of the singular development of rose spots may thus be conjectured. In adults the etiologic agent localizes itself chiefly in the intestine. This happens, to a small extent, in children and the bacteremia, with a more or less pronounced exanthem, is the most prominent symptom. In contrast to these cases, those showing clearly localized intestinal symptoms, which Lehfeld described as the colitic form and to which one can assign the cases of Goebel and Ulmer in which the agent was identified as paratyphoid B, show no rose spots. He who would draw clinical parallels may think of the conditions, antagonistic to a certain degree, in the periphery and in the viscera in tuberculosis and syphilis.

MIXED INFECTION OF SCARLET FEVER AND DIPHTHERIA IN TALLINN-RAVEL (ESTHONIA), 1926-1927. FELIX VON BORMANN, Ztschr. f. Kinderh. **46**:233 (July) 1928.

In the course of the great epidemic of scarlet fever in Tallinn-Ravel, in the autumn of 1926 and the spring of 1927, there frequently occurred a mixed infection of scarlet fever and diphtheria which was coupled with a high mortality rate (from 20 to 100 per cent). Typical cases of scarlet fever at that time showed no malignant condition, and typical cases of diphtheria were associated neither with an increased morbidity nor with mortality. Snuffles and swelling of the glands under the jaw were usually seen as early symptoms of the mixed infection, but, on the other hand, the throat picture was without significance. Later, a symptom complex developed, consisting of a purulent rhinitis, an exudate from

the throat, usually necrotic, or an edematous swelling of the tonsils and a phlegmonous infiltration of the glands of the lower jaw and neck. An extensive angina necroticans and a picture resembling Ludwig's angina flared up. The augmenting of scarlet fever by diphtheria heavily increased the number of early and late complications of scarlet fever. The number of typical complications of diphtheria were few. Cases of croup were infrequent just as they always are when diphtheria is associated with a necrotic process in the throat. When a mixed infection was suspected, the Klebs-Loeffler bacillus was usually found in the nose and throat. Since some cases of pure diphtheria appeared among the cases of mixed infection, and because the cases in which the Klebs-Loeffler bacillus was found were usually cases of diphtheria and, finally, because complications characteristic of diphtheria came under observation, one may assume that the cases described were mixed infections of scarlet fever and true diphtheria. Often the Klebs-Loeffler bacilli were demonstrated only with difficulty because they were sparse, which apparently explains the extraordinarily small amount of the extension of the diphtheria to other children. In about one fourth of the cases, bacilli were not found after repeated search, but in a fraction of these the bacilli came to light at autopsy. These circumstances as well as the same clinical condition in such cases with proved mixed infection, lead to the conclusion that only the clinical picture, at least according to the experience of the investigators, can determine the diagnosis of a mixed infection; the bacterial picture plays only a supporting part. Every kind of nonspecific therapy, including protein therapy, failed completely. Neither diphtheria antitoxin nor scarlet fever serum by itself helped greatly. Only with combined injection of scarlet fever convalescent serum, (obtained during the first four or five days of the sickness) and massive doses of diphtheritic antitoxin was it possible to lower the mortality to any great degree.

AN EPIDEMIC OF GRIP CAUSED BY THE BACILLUS OF INFLUENZA IN THE PEDIATRIC CLINIC OF THE UNIVERSITY OF HALLE. E. BARTH, R. HERBST and H. NEUMANN, Ztschr. f. Kinderh. **46**:286 (July) 1928.

In relation to an epidemic of grip in the Pediatric Clinic of the University of Halle in the spring of 1927, which affected almost the whole personnel and numerous children, abundant bacteriologic studies were made on both adults and children. *Bacillus influenzae* (Pfeiffer) was grown almost regularly from the sputum of the adults and often from that of the children and infants; for this reason in relation to other circumstances, this organism is declared to be the etiologic agent of this epidemic of grip. It was sought to establish a characteristic picture of the disease caused by this bacillus; that is, severe general symptoms, the failure of real local symptoms except circumscribed redness of the palatal arch, a cough like that of pertussis and no complications of the urinary passages, of the ears or of the intestinal tract. In the handling of such an epidemic the nursing personnel, especially those with nasal discharges, must be examined for the presence of the Pfeiffer bacillus; those in whom the bacillus is found must be supplied with face masks and kept away from delicate children. The children who react positively should be isolated as far as possible. On prophylactic grounds it is proposed, without regard for the etiologic point of view, to reserve the term "influenza vera" not for pandemic grip but for all sicknesses caused by the bacillus of influenza.

PRIMARY EPIDEMIC PANCREATITIS. J. K. FRIEDJUNG, Ztschr. f. Kinderh. **46**:303 (July) 1928.

The observation here reported shows that in an epidemic of mumps the pancreas may take part not only as a sequela but as the manifestation of the disease. The subsequent swelling of the parotid, though the diagnosis would have been the same without it in the case cited, and the whole course of the disease prove the diagnosis. Every one should be prepared to recognize an epidemic of primary pancreatitis.

Gallie and Brown operated in a case of this sort. The author reports this case because in the literature on parotitis epidemica such an entity appears not to be recognized.

COMBINED OPTOCHINE VACCINE THERAPY IN CEREBROSPINAL MENINGITIS. E. RUBEL, Ztschr. f. Kinderh. **46**:391 (Sept.) 1928.

How good the method reported by Rubel is and how correct the optimum dosage of optochine vaccine, the future will tell, but the attempt to combine chemotherapy with vaccine therapy will lead possibly, under favorable conditions, to a new chapter in the history of medicine. The idea of influencing the reticulo-endothelial system in this fashion deserves confirmation from clinical and experimental material.

IMMUNOBIOLOGIC STUDIES ON THE SECOND OCCURRENCE OF SCARLET FEVER. H. BAAR, A. GRABENHOFER and G. KRAUSZ, Ztschr. f. Kinderh. **46**:423 (Sept.) 1928.

The immunobiology of the second attack of scarlet fever was studied by the use of the indirect blanching phenomenon, partly with the help of the Dick test. Of thirteen cases showing residual symptoms of scarlet fever, the indirect test gave positive results in ten. The assumption of an allergic genesis is plausible for the return of scarlet fever and perhaps for nephritis. In cases of lymphadenitis, otitis media and other complications of scarlet fever, no sure dependence exists on immunity as measured by the indirect blanching test.

EMERSON, Boston.

BRADYCARDIA AND BLOOD PRESSURE IN DIPHTHERIA. N. WAIZUMI, J. Pediat. (Tokyo), Dec. 20, 1928, no. 343, p. 2135.

The author attempts to correlate the phenomenon of bradycardia with blood pressure in children affected with clinical diphtheria. Of 277 patients with diphtheria admitted into the Keio University Hospital, in whom positive cultures were obtained, only 8 developed bradycardia; all these patients had laryngeal diphtheria. All received 500 units of antitoxin per kilogram of body weight within the first forty-eight hours after the appearance of the first symptom. The associated symptoms of bradycardia were extreme loss of appetite, malaise, thoracic pain, enlargement of the cervical lymph glands, arrhythmia with occasional heart block, pallor, apathy and occasionally nausea and vomiting, as well as cyanosis of the extremities. From the prognostic standpoint, it is worthy of note that all the cases of bradycardia which resulted fatally showed a lowering of the blood pressure, while the cases of bradycardia in which a cure was effected showed no such lowering.

SEVERE COMPLICATIONS OF PERTUSSIS. M. SAKAUCHI, J. Pediat. (Tokyo), Dec. 29, 1928, no. 343, p. 2187.

The author mentions three rather severe complications arising during the course of pertussis. The first is a total inability to nurse, which he saw in an infant, aged 4 months, and which lasted more than two weeks. During this time, nourishment was maintained by nutrient enemas. He states that the usual method of treatment had no influence in overcoming this condition. The second form is an apneic paroxysm, which comes at varying intervals and is characterized by a total cessation of respiration and pulsation, with more or less marked cyanosis. The condition is a veritable temporary death, and usually lasts from a few to ten minutes. The author was satisfied that this was not a case of tetany, as usual signs of spasmophilia were absent. The third complication is a hemiplegia which seems to have its origin in toxemia of pertussis. The so-called pertussis encephalopathy described by the German writers closely resembles this condition.

KATO, Los Angeles.

Chronic Infections

OBSERVATIONS ON SOME UNUSUAL CASES OF JOINT TUBERCULOSIS. C. W. BLACKETT, Am. J. Roentgenol. **16**:427 (Nov.) 1926.

The author reports five cases, which he regards as tuberculosis of the bone, but which show, in the roentgenograms, deep pockets of destruction extending from the cavity of the joint into the bone with little atrophy and none of the blurred outline or "fogginess" so common with tuberculous joints.

AN ATTEMPT TO APPRAISE THE ROENTGENOLOGICAL METHOD OF DIAGNOSIS IN PULMONARY TUBERCULOSIS. FRANK S. BISSELL, Am. J. Roentgenol. **16**:544 (Dec.) 1926.

A careful review of the completed histories of 126 cases of clinically diagnosed tuberculosis, despite negative roentgen reports, showed that at least 124 cases presented no conclusive or satisfactory evidence of healed or active pulmonary tuberculosis. Follow-ups of 96 patients in whom the roentgenologic diagnosis of minimal tuberculosis was made revealed 87 cases of pulmonary tuberculosis of the chronic, active type, and 9 cases of arrested pulmonary tuberculosis. Pneumonoconiosis, pulmonary changes in cardiac disease, Hodgkin's disease and metastatic malignant disease were found in cases in which an erroneous roentgenologic diagnosis of advanced or moderately advanced tuberculosis had been made. To avoid error, cooperation of the clinician and roentgenologist must be secured. Roentgen evidence as to activity or quiescence of a lesion is not conclusive. Basal tuberculosis having its origin in one base is not uncommon in the adult, but the lesion spreads rapidly to the upper fields.

STULIK, Chicago.

A STUDY OF TUBERCULOUS LESIONS IN THE LUNG OF A NEGRO CHILD NINE WEEKS OLD. WILLIAM SNOW MILLER, Am. Rev. Tuberc. **18**:373 (Oct.) 1928.

The gross pathologic changes found were enlargement of the tracheobronchial lymph nodes, with extensive caseation of those along the left bronchus. The surfaces of the lungs were smooth with no adhesions. Both lungs were studded with tubercles, varying from a point just visible to one 1.5 mm. in diameter. A careful study was made of the margin of the left lower lobe by reconstruction. Miliary tubercles were the only lesions found. The infection was conveyed from some undetermined source through the arterial blood stream. The tubercles developed in the capillary bed between the pulmonary artery and the pulmonary vein. The primary infection seemed to be in the lymphoid tissue associated with the pulmonary veins: this receives its blood supply from the pulmonary artery. The lymphatics were not involved in the tuberculous lesions. All the valves found in the lymphatics were situated less than 2 mm. below the surface of the pleura and opened toward the pleura. This means that from a narrow peripheral zone of the lung, the lymph must drain toward the pleura, but leaves unsettled the direction of flow from deeper portions, although it must be assumed that from the central portion, flow is toward the hilum.

MILIARY TUBERCULOSIS IN CHILDREN. JOSEPH GREENGARD, Am. Rev. Tuberc. **18**:392 (Oct.) 1928.

Fifty-four cases of miliary tuberculosis were studied clinically; thirty-five of the cases came to autopsy. Tuberculous meningitis was found in 80 per cent of the cases in which autopsy was performed. Caseation of the tracheobronchial lymph nodes was a constant pathologic observation. Lesions in the lungs which appeared to represent the primary nidus of infection were found in twenty-four cases. Pulmonary cavitation was noted in five. Caseation of the mesenteric lymph nodes was present in twenty-four cases and was unaccompanied by advanced tuberculosis of the gastro-intestinal tract in most instances. Suppurative otitis media was found in eight cases of meningeal tuberculosis. Smears of the pus from the ears of several of the patients demonstrated the presence of tubercle bacilli.

THE INCIDENCE OF PLEURAL LESIONS AS SHOWN BY ROENTGENOGRAPHS IN CHILDREN KNOWN TO BE TUBERCULOUS. LLOYD B. DICKEY and L. H. GARLAND, Am. Rev. Tuberc. **18**:404 (Oct.) 1928.

In a series of roentgenograms of the chest of 327 children known to be tuberculous and of a control series of fifty patients, a surprisingly high incidence of pleural lesions could be demonstrated. In the group of children aged 1 to 2 years, pleural lesions were demonstrated in 58 per cent. No relation could be shown between pleural lesions and enlargement of the lymph nodes of the hilum.

Pleurisy with effusion is usually interpreted easily. Pleural adhesions can usually be demonstrated only at the costophrenic or cardiophrenic angles. Thickening of the pleura will always show in a good roentgenogram when there is a less dense medium on either side, as in thickened interlobar septums. Parietal thickening, at least when it is greater than 0.5 mm., should be seen in a good anteroposterior projection; the areated tissue of the lung can be seen separated from the bony wall of the chest by a thin homogeneous grayness. Apical pleural thickening shows as a thin, curved line of density running parallel with the pulmonary substance but not merging with the rib shadows as they turn toward the vertebral column, nor with the edge of the scapular shadow at its upper vertebral end. It is rarely possible to demonstrate mediastinal and basal pleural thickening.

SMITH, Ogden, Utah.

PRENATAL CLINICS AND THE PREVENTION OF CONGENITAL SYPHILIS. VALERIA H. PARKER, J. Social Hyg. **15**:70 (Feb.) 1929.

The medical women's national association appointed a special subcommittee to make a study of the activities of the prenatal clinics in the matter of diagnosis and treatment of syphilitic infections in the pregnant women under treatment there.

Dr. Parker gives some interesting figures in making out the report of the committee. She cites the work of Dr. J. Whitridge Williams, who made a study of 705 fetal deaths occurring in 10,000 consecutive admissions. Twenty-six per cent of these deaths were attributable to syphilis; 14 per cent were in children of white mothers, and 35 per cent in negro infants.

When treatment was instituted, the figures were lowered for both mother and child. Only 6.7 per cent of the children of women who received adequate treatment showed any manifestations of syphilis. The earlier the mothers are treated, the greater are the chances for the child to be free from syphilitic infection.

Dr. Parker advocates a continuous treatment of syphilitic mothers and fathers, a Wassermann test on every expectant mother, and a more thorough care of the pregnant mother by the private physician.

YAMPOLSKY, Atlanta.

THERAPEUTIC PNEUMOTHORAX IN PULMONARY TUBERCULOUS CHILDREN. P. F. ARMAND-DELILLE, M. J. & Rec. **123**:113 (Jan. 20) 1926.

From 1922 to the end of 1924, the author was in charge of a ward of tuberculous children at the Debrousse Hospital, in which were received all the cases of pulmonary tuberculosis from the children's hospitals in Paris. At first, pneumothorax was practiced only in far advanced cases showing cavities, rapid caseation or hemoptysis. Later, it was used in all cases in which x-ray observations showed one lung to be affected, and in which tubercle bacilli were found in the sputum or gastric contents. The injections had to be repeated every week, and care was taken not to increase the pressure so as to obtain a positive pressure in the thorax. The Kuss apparatus was used. No untoward results were seen; occasionally there was some subcutaneous emphysema, and in 25 per cent of the cases some fluid formed in the pleural cavity, but, usually, this was spontaneously absorbed. Fifty-five per cent of the patients treated in 1922 and 1923 are definitely cured. Their general condition is excellent, and no tubercle bacilli can be found in the sputum. No other method of treatment up to the present time has afforded such gratifying results.

LESLIE, Evanston.

ON PREVENTIVE VACCINATION OF THE NEWLY BORN AGAINST TUBERCULOSIS BY B. C. G. A. CALMETTE, Brit. J. Tuberc. **12**:161 (Oct.) 1928.

In tuberculosis, as in syphilis, immunity, interpreted as a resistance to reinfection, appears only when the organism harbors elements of the specific parasite, and under the express condition that these elements are living, in sufficient number, and that their virulence is so diminished that they will not produce grave lesions or functional troubles incompatible with life. Immunity against infection with tuberculosis results from the presence of some living tubercle bacilli in the organism. It has been established that in subjects slightly infected with tuberculosis, with lesions that are not extensive, a grave form of tuberculosis never develops when a new infection occurs, and that the tuberculosis of reinfection always has the appearance of a chronic sickness.

The special strain of avirulent tubercle bacilli developed by Calmette and Guerin (B.C.G.), while keeping its original antigenic properties, has definitely lost all aptitude for actively creating tuberculous lesions transmissible by inoculation. No experimenter has succeeded in restoring its virulence sufficiently to infect even a guinea-pig. The vaccine is prepared by placing an emulsion of these bacilli into a binding fluid in such a manner that each dose contains 400 million living germs. It is administered during the first ten days following birth, in three successive doses at forty-eight hour intervals. Oral administration of the vaccine is effective since it has been shown that until about the fifteenth day after birth, the intestine of the infant absorbs microbes and antitoxin with great facility.

Up to July 1, 1928, 96,000 children have been vaccinated in France and 45,000 in French Indo-China alone. A careful investigation of the merits of the procedure is now being made by a commission organized by the Section of Hygiene of the League of Nations. The author affirms, however, that this method of vaccination, when applied to newly born children, is inoffensive and appears to be really efficacious.

SMITH, Ogden, Utah.

THE PATHOLOGY OF PULMONARY AND BRONCHIAL GLAND TUBERCULOSIS IN INFANCY AND CHILDHOOD. P. F. ARMAND-DELILLE and C. LESTOCQUOY, Tubercle **9**:359 (May) 1928.

The conclusions here presented are based on clinical, roentgen and autopsy studies in eighty-four cases. It was possible to study the early changes in pulmonary tuberculosis in infants who died from some intercurrent infection while under observation. In order that the observations at autopsy might be carefully checked with the x-rays, the contents of the chest were placed in a plaster cast which had exactly the form of the thoracic cavity of a child of the same age, and were allowed to harden. After two weeks the block was removed, sectioned and studied. The authors came to the following conclusions: 1. Tuberculous glands are always enlarged. When they occur in the mediastinum they are not detected by the x-rays because they are masked by the shadows of the heart, aorta and superior vena cava; when they occur along the trachea, however, they are readily shown. 2. The primary inoculation is demonstrable in nearly every case from a study of the postmortem sections, but it is rarely seen in the roentgenogram because it is so frequently behind the shadow of the heart, liver or spleen. 3. Good roentgenograms may reveal the presence of miliary tuberculosis early in the disease, often before any other characteristic sign or symptom has appeared. 4. The so-called lobar shadow is the one found most frequently in roentgenograms of the chest of tuberculous infants. It may be caused by primary hepatization, secondary hepatization, caseation or even by splenopneumonia. Shadows which have been considered perihilar condensations represent in reality the first stages of a lobar bronchopneumonic invasion. In some cases the shadows, even when tubercle bacilli have been demonstrated in the sputum, gradually disappear, showing that healing may occur in rare cases. In most instances the shadows increase progressively, going on to invade other lobes or even the opposite lung. When such changes are seen to occur, the indication is for collapse therapy by means of artificial pneumothorax.

LESLIE, Evanston.

LARYNGEAL TUBERCULOSIS IN OLDER CHILDREN; THE INFLUENCE OF ARTIFICIAL PNEUMOTHORAX ON ITS CURE. P. F. ARMAND-DELILLE and H. CABOCHE, Bull. et mém. Soc. méd. d. hôp. de Paris **51**:631 (May) 1927.

Four cases showing definite laryngeal tuberculosis are reported. Pulmonary tuberculosis was also present. In one case the progressive laryngeal changes were followed for a period of eight months, at the end of which time pneumothorax was instituted. Six months later, the larynx appeared normal. In two cases pneumothorax was instituted immediately, and in both there was progressive healing of the larynx. In the fourth case, the condition of the larynx was greatly improved when death from hemorrhage intervened. The tuberculous nature of the lesions was confirmed at autopsy. The beneficial effect of the pneumothorax would seem to be due to the disappearance of the cough, which lessens the possibility of reinoculation and of trauma to the larynx.

SIMULTANEOUS BILATERAL PNEUMOTHORAX IN PULMONARY TUBERCULOSIS IN CHILDREN. P. F. ARMAND-DELILLE, Bull. et mém. Soc. méd. d. hôp. de Paris **51**:1693 (Dec. 29) 1927.

At the insistence of the parents, bilateral pneumothorax was practiced in two private patients, aged 3 and 13 years, respectively, who showed definite signs of involvement of both lungs. Following the injections, the children who had had fever, cough and loss of weight began to show immediate improvement, which continued to the time the article was written. Although roentgen examination showed almost normal parenchyma of the lungs after a year and a half of observation, it was thought advisable to continue to collapse the lungs until the third year of treatment was completed. Similar results were obtained in the treatment for bilateral pulmonary tuberculosis in cases in the wards, with no harmful results. Children who almost certainly would have progressed rapidly toward a fatal outcome showed marked improvement in their general condition, loss of fever and cough, an absence of tubercle bacilli and healing of the parenchyma of the lung.

LESLIE, Evanston.

FOUR NEW CASES OF ACRODYNIA: CONJUNCTIVITIS AND MENTAL DISTURBANCES. H. JANET and J. DAYRAS, Bull. Soc. de pédiat de Paris **8**:400 (Oct.) 1928.

Conjunctivitis, the chief complaint in the first case, was a frequent occurrence in the cases described by Chardon in Paris in 1828. In the second case, outbursts of rage and finally a maniacal state preceded and dominated the other symptoms. In the third case, asthenia was so profound that the mother suspected that the child was paralyzed.

MENINGITIS DUE TO HEREDITARY SYPHILIS. M. HEUYER and BACH, Bull. Soc. de pédiat. de Paris **8**:413 (Oct.) 1928.

A boy, aged 4 years, was first thought to have tuberculous meningitis. Stigmas of syphilis in him and in his father, however, and great improvement after antisyphilitic treatment, suggest the diagnosis of syphilitic meningitis, although the Wassermann reaction was negative in both the blood and the spinal fluid. Some of the French literature is cited.

CLAUSEN, Rochester, N. Y.

TUBERCULOUS LOBES IN THE LUNGS OF INFANTS. P. F. ARMAND-DELILLE and C. LESTOCQUOY, Gaz. méd. de France **2**:214 (May) 1928.

Contrary to the opinion that localized tuberculosis is the rule in the adult and the exception in the child, the authors found that in seventy-one out of ninety-six cases studied, the roentgenographic shadow was limited to one lobe of the lung. Of fifty-five cases in which the tubercle bacillus was recovered, thirty-two showed localized shadows. Occasionally, tubercle bacilli may be recovered when

the roentgenogram is apparently negative. In small children the organism must be looked for in the washings of the stomach obtained early in the morning.

When checked by means of autopsy observations, the localized shadow is seen to represent a variety of lesions. One type consists of a sort of hepatization of the whole lobe around a center of caseating nodules. In another type the changes in the affected lobe are bronchopneumonic in pattern. A complete caseation of the lobe may also be seen, and in a few cases an ulcerative tuberculosis with the formation of a cavity was found.

LESLIE, Evanston.

DOCUMENTS OF ASSISTANCE IN THE STUDY OF INFANTILE TUBERCULOSIS FROM BIRTH TO SIX MONTHS. H. BARBIER, Rev. de la Tuberc. **9**:507 (Aug.) 1928.

In this paper the history and the clinical and autopsy data are abstracted in more than fifty cases of tuberculosis occurring in infancy, illustrating the diverse manifestations of the disease during this period of life. In spite of the variable evolution of the disease and the difficulty of classification into definite types, the following groups may be recognized:

Patients who succumb within a few days with no lesions except congestion of the lungs and especially of the meninges, or with apparently insignificant areas of caseation. Death occurs from an overwhelming toxemia before sufficient time has elapsed for the development of a typical initial lesion.

A group with acute symptoms, characterized by high fever, alveolitis, bronchopneumonia and widely disseminated formation of tubercles.

Groups in which respiratory symptoms, cough, oppression, suffocation and cyanosis predominate on the one hand, and on the other, digestive symptoms, dyspepsia and enteritis.

A group of toxic patients characterized by stupor, anemia, cyanosis, malnutrition, loss of weight and progressive cachexia.

A group simulating pseudoleukemic anemia.

Numerous cases in which the disease assumes a septic character, with pyodermia, involvement of the mucous membranes and infections of the ears. A certain number of these patients survive the initial invasion but continue a miserable existence with dyspepsias and atrophies, ending in cachexia and hypothermia.

Finally there are those cases in which the disease seems to become stabilized and in which healing takes place, interrupted, however, by more or less brief periods of activity.

SMITH, Ogden, Utah.

HEALTH VACATIONS FOR THE PRETUBERCULOUS CHILD AS PRACTICED BY THE AUSTRIAN STATE INSURANCE. LEOPOLD MOLL, Gesundhtsfürs. f. d. Kindesalt. **3**:559, 1928.

Moll describes the organization of vacations for children from 4 to 14 years of age who are exposed to tuberculous infection or whose physical condition threatens a reactivation. The children were sent to preventoriums which were under the constant supervision of a full-time physician and which were located either in the Alpine regions of Austria or on the German coasts of the North Sea and the Baltic Ocean. A history of rheumatism or disease of the heart or kidneys was regarded as a contraindication for a vacation at the seashore; such children were sent to the mountains. Children of the pale, fat type, described by the Germans as pastös, were likewise more benefited by wooded and mountainous localities. Otitis media frequently flared up and led to serious mastoid complications during a stay at the seashore, so that children with this condition were sent to Alpine districts. Children with latent tuberculosis of the hilum improved best at the seashore. These patients, however, must be watched for any indication of activity of the disease; in case it occurs, the child must be returned to preventoriums located in a high altitude. Moll believes that excellent results were obtained. The children had better appetites and an increased resistance to

infections of the upper respiratory tract, on their return. Considerable education of the parents was apparently carried out by social service nurses, the value of which Moll perhaps underestimates in this article.

REICHLE, Cleveland.

A MODIFICATION OF THE WASSERMANN REACTION: THE MICROMETHOD AND ITS SIGNIFICANCE FOR PEDIATRIC CLINICS. NIEDERWEISER and LAUTER, Ztschr. f. Kinderh. **46**:263 (July) 1928.

The micromethod for obtaining the Wassermann reaction was described by Dohnal in 1923 and simplified by Niederweiser. The present workers should like to find by testing this method that it is one which can be used when it is necessary to get along with a small amount of blood. This procedure is all the more essential because the infant already harmed by the syphilitic virus has a weakened blood-forming apparatus and would be further harmed by a great withdrawal of blood, though naturally the physician wishes to orient himself frequently as to the status of his treatment. This method is communicated with no established conclusions but with a hope that the work will be confirmed and the method improved.

EMERSON, Boston.

Internal Diseases

AN EPIDEMIC OF RHEUMATISM AT A CARDIAC CAMP. R. I. HILLER and IRVING GRAEF, Am. Heart J. **3**:271 (Feb.) 1928.

A survey of an epidemic of rheumatism is presented in which nine cases of rheumatism, one of chorea and one of acute tonsillitis developed during the course of four weeks in a camp of thirty-eight patients convalescing from heart disease.

This is interesting in the light of studies to isolate a specific virus, and in the conclusion of Boas and Schwarts "that rheumatic fever has many of the characteristics of other infectious diseases with a low degree of contagiousness, but that at times and under special conditions it may assume epidemic proportions." In this group, although inclement weather played a part in the incidence, communicability undoubtedly was a factor.

MANNING, Santa Barbara, Calif.

OSTEOPETROSIS. ROLLA G. KARSHNER, Am. J. Roentgenol. **16**:405 (Nov.) 1926.

Osteopetrosis is an hereditary disease, essentially a disturbance of the mesenchyme, manifesting itself primarily by extraordinary thickness and density of the cortical portion of the osseous system at the expense of the medullary portion, and giving rise to a diversity of secondary characteristics, such as multiple fractures, epiphyseal deformities, physical underdevelopment, hydrocephalus, optic atrophy, imperfect dentition, anemia, various leukemic conditions and metaplasia of bone marrow elements leading to enlargement of the liver, spleen and lymph nodes. The author cites four of his own cases and reviews eighteen from the literature.

There is a disturbed calcium metabolism with increased ability to bind calcium. Syphilis is excluded and vitamins, apparently, are not involved. The cortical bone increases in size with obliteration of the spongiosa; microscopically, it resembles normal compact bone. Because of obliteration of bone marrow, metaplasia of blood-forming elements with enlargement of the spleen, liver and glands occurs, resembling anemia and leukemia in severe cases. The typical facies consists of a broad face, wideset eyes, no slant, no epicanthal fold, sunken root of the nose with a broad, upturned tip and round nares set far apart. The lips are thick, the mouth is closed, the tongue does not protrude, hair is abundant, teeth are bad and the skin has senile wrinkling. Roentgen observations show a typical density of all bones; differentiation of the condition from other bone dystrophies is not difficult. The disease is chronic and often progressively fatal, though in some the disease seems to be arrested. Treatment is prophylactic; it consists of guarding against trauma and dental infection, and avoiding substances known to promote bone growth, such as arsenic, phosphorus and cod liver oil. A bibliography is included in the article.

RESOLUTION IN PNEUMONIC CONSOLIDATIONS. R. G. ALLISON, Am. J. Roentgenol. **16**:549 (Dec.) 1926.

The typical mottling described by Cole may be regarded as the earliest definite roentgen sign of pulmonary tuberculosis. Pulmonary tuberculosis may be diagnosed earlier, but the shadows are not pathognomonic. Remarkable resolution, even to complete disappearance of a tuberculous lesion, can take place in a few months. Indications for therapeutic abortion can often be seen in a single set of roentgenograms of the chest, but artificial sterilization should never be advised until a period of observation has shown that the lesion will not undergo resolution. Most observers agree, however, that a negative x-ray plate is of definite value in excluding pulmonary tuberculosis, although a positive diagnosis can often be made by other means.

STULIK, Chicago.

FOREIGN BODIES IN THE STOMACH AND IN THE INTESTINES. M. C. MYERSON, Arch. Otolaryng. **8**:675 (Dec.) 1928.

Foreign bodies in the gastro-intestinal tract are frequently seen, especially in children less than 10 years of age. Of thirty-nine patients twenty-one were less than 5 years of age, and eleven were from 5 to 10 years of age. In fourteen cases, pins of various types were the objects swallowed. Thirty-six of the thirty-nine objects were passed with the stool; the other 3 were removed by gastrotomy. Eighty-two per cent of those passed were pointed.

Foreign bodies that are swallowed may be regurgitated, may pass through the length of the gastro-intestinal tract, or, in a few cases, may perforate the tissues.

The value of feeding thick cereals is questionable. Cathartics are more likely to be harmful than harmless. Operative intervention is to be used conservatively, especially in infants, since operations on the stomach of children less than 1 year old have a high mortality rate. If possible, gastroscopy is the method of choice; when this is impossible, watchful waiting is the best policy.

BARNETT, Chicago.

ABDOMINAL PAIN IN CHILDREN WITH UPPER RESPIRATORY INFECTION. H. B. HAMILTON, M. Clin. N. Amer. **12**:495 (Sept.) 1928.

The most common variety of abdominal pain encountered by the pediatrician is that which accompanies respiratory infections. The cause of the pain occurring in pneumonic processes with pleural involvment is probably the same mechanism which functions in Head's zones. When the upper respiratory tract alone is involved, the cause is more obscure. Hamilton suggests that in these cases the intestinal musculature may be affected in the same manner that the general muscular system is involved in acute grippal infections.

The pain in these cases differs from that due to intra-abdominal inflammation in that the tenderness is less marked and more diffuse. There is more complaint of pain than of tenderness. While abdominal pain is common in respiratory infections in children, vomiting is almost universal. Continuation of the vomiting for more than two days, however, is less dependent on disease than on the measures often used for its relief, such as cathartics and other drugs, and on the too early administration of food.

CASES OF VOMITING IN CHILDREN DUE TO MECHANICAL OBSTRUCTION AT THE PYLORUS; CASES OF VOMITING IN CHILDREN DUE TO TOXEMIA. H. M. MCCLANAHAN and J. A. HENSKE, M. Clin. N. Amer. **12**:537 (Sept.) 1928.

Cases illustrating these types of vomiting are reported. In the first group, due to pyloric stenosis, diagnosis is possible from history and physical examination, without laboratory aid, in 90 per cent of the cases. Feeding with thick gruel may be given a trial if the patient is seen early, if dehydration is absent, if the child is within 25 per cent of its normal weight and if complete cooperation

of the mother is possible. Otherwise, the Fredet-Rammstedt operation is most likely to result in a rapid and satisfactory cure.

In the second group, attention is directed to the frequency with which infections of the middle ear and mastoid underlie acute and serious gastro-intestinal disturbances. When an infant on a diet which has been carefully planned and which has stood the test of a fair trial suddenly develops acute digestive symptoms, the food should be blamed only after an exhaustive search for parenteral infections has proved fruitless.

SMITH, Ogden, Utah.

HEART DISEASES IN SCHOOL CHILDREN. D. BREWER, Arch. Dis. Childhood **3**:277 (Dec.) 1928.

An abnormal condition of the heart was found in 36 per thousand of 25,000 children examined. This included functional murmurs, which constituted the condition in 28 per thousand.

PETERMAN, Milwaukee.

CIRRHOSIS OF THE LIVER. R. CECIL WALL, Proc. Roy. Soc. Med. **21**:1320 (June) 1928.

The author reports a case of cirrhosis of the liver in a boy, aged 6 years. The etiology of the cirrhosis was not known, but the boy often had shared drinks of gin with his father.

WILLIAMSON, New Orleans.

NONHEREDITARY CRANIAL DYSOSTOSIS. M. HEUYER and BACH, Bull. Soc. de pédiat. de Paris **8**:411 (Oct.) 1928.

The authors describe a case resembling oxycephaly, with deformities of the legs similar to those of rickets and with progressive primary optic atrophy. A brief bibliography of the French literature is appended.

CLAUSEN, Rochester, N. Y.

LOW HUMIDITY SYNDROME. G. MOURIQUAND and CHARPENTIER, Nourrisson **16**:372 (Nov.) 1928.

In the vicinity of Lyons, the winds from the south are accompanied by a low barometric pressure and a low humidity. When these winds prevail, the authors have noted a syndrome in infants characterized by the symptoms of acute dehydration (without diarrhea), sunken eyes, drawn facies, doughy skin, rigidity and pain. Elevations of temperature up to 41 C. (105.8 F.) and above in the severe forms precede death. The victims are usually infants of poor nutrition. Necropsies have revealed no explanation. In this locality meteorologic observations normally show a humidity of 50 at midday and of 90 at night. With the wind from the Midi the diurnal humidity is about 30 and the nocturnal, below 40. On May 30, 1927, six infants were affected with the condition; three of these died. The authors are convinced of the correctness of their deductions from the results obtained by prophylaxis. If when a south wind blows the air in the wards is cooled and humidified, the infants are not affected with any of the foregoing symptoms.

MCCLELLAND, Cleveland.

BACTERIOLOGY AND VACCINE THERAPY IN BRONCHOPNEUMONIA. A. DUPONT, Arch. latino-am. de pediat. **22**:505, 1928.

The usual causative agent in bronchopneumonia is the pneumococcus. In addition and with about equal frequency, *Streptococcus hemolyticus* and the enterococcus are found. All other organisms found are of minor importance.

The author recommends the use of a vaccine prepared according to the method of Weill and Dufort. These authors had observed that between 70 and 75 per cent of patients with bronchopneumonia respond favorably to the use of a vaccine com-

posed of a combination of pneumococci and enterococci but in no case responded to a vaccine made from streptococci. This is probably due to the fact that the streptococcus is not an organism of a single type but occurs in many forms.

Three injections of 1 cc. of vaccine are given, each cubic centimeter containing 400 million pneumococci and enterococci and 200 million staphylococci and *Bacillus tetragenos*. The results with this therapy have been quite striking. The improvement has been rapid and definite, and the mortality rate nearly 50 per cent less in the treated patients than in those untreated.

SCHLUTZ, Minneapolis.

THE DIAGNOSIS OF SUBPHRENIC ABSCESSES BY THE ROENTGEN RAYS. WALTER SAUER, Ztschr. f. Kinderh. **46**:314 (Sept.) 1928.

In association with a follicular tonsillitis, three subphrenic abscesses developed in a child, aged 2½ years. Roentgen examination in different positions and at different levels led to accurate diagnosis and localization. After operative treatment of the subphrenic abscesses, gangrenous appendicitis followed with a perityphlitic abscess. Etiologically, Sauer took a lymphogenous infection for the cause of the subphrenic abscesses which subsided at the time of the operation. A renewed acute attack of chronic appendicitis led to the perityphlitis and the gangrenous appendicitis.

HYPOPHYSEAL MAP-SKULL. T. BREHME, Ztschr. f. Kinderh. **46**:401 (Sept.) 1928.

A case is added to the ten cases of map-skull (defects of the flat bones in combination with hypophyseal disturbances, diabetes insipidus or dystrophia adiposo genitalis) described in the literature. The disease is looked on as caused primarily by the hypophysis.

EMERSON, Boston.

Nervous Diseases

AMAUROTIC FAMILY IDIOCY AND GENERAL LIPOID DEGENERATION. B. SACHS, Arch. Neurol. & Psychiat. **21**:247 (Feb.) 1929.

Clinical and pathologic studies have revealed a surprising relationship between amaurotic family idiocy and another group of diseases — Gaucher's disease and a familial and fatal disease of infancy showing great predilection for the Hebrew race and bearing some, if not complete, resemblance to Gaucher's disease. This disease is spoken of as a lipoid cellular splenohepatomegally, or, as Bloom called it, lipoid histiocytosis (type Niemann), an infantile type now known as the "Niemann-Pick type" in contradistinction to the Gaucher type. Both types would appear to be variants of a general lipoid cellular degeneration with enlargement of the spleen and liver. The author stated that the disease which he has identified for so many years seems to have acquired additional interest, and he has brought up this matter in the hope that any one who has occasion to see typical cases of amaurotic idiocy will pay especial attention to the careful microscopic examination of every organ and tissue of the body, even including the bone marrow.

INTRA-UTERINE POLIOMYELITIS; A REPORT OF A CASE IN WHICH A RECRUDESCENCE OF SYMPTOMS OCCURRED AFTER FIFTY YEARS. CHARLES S. POTTS, Arch. Neurol. & Psychiat. **21**:288 (Feb.) 1929.

From a review of the literature, the author concludes that as it has been shown that epidemic encephalitis sometimes may infect a fetus if the mother has the disease, and also that encephalitis in utero may be acquired from other infections, may not poliomyelitis be similarly transmitted? It must be remembered that this disease may be present, but that the symptoms may be so mild as not to attract attention. It is conceivable that a mother in this state might transmit the disease. In the cases reported by Globus, Patterson and Carmichael and

Batten, the mothers were not ill. The experiments of Levaditi are important in this connection.

That the patient described by Potts had poliomyelitis, as far as clinical symptoms and pathologic changes are concerned, is evident. That these symptoms were present when he was born seems probable. Whether or not they were due to the specific virus of poliomyelitis, to some other form of infection or to hereditary syphilis is doubtful in this case. It seems likely, however, that a true anterior poliomyelitis may occur in utero, although it must be rare.

RECURRENCE OF STUTTERING FOLLOWING SHIFT FROM NORMAL TO MIRROR WRITING. LEE EDWARD TRAVIS, Arch. Neurol. & Psychiat. **21**:388 (Feb.) 1929.

The author's case was that of a medical student, aged 25, who wrote so poorly that he could not read his own writing. In the training process involved, he was taught mirror writing, which resulted in the development of stuttering. Travis explains this by the assumption that articulate speech had been associated with writing of the usual orientation, that is, to the right, although it is obvious that a close bond had not been established between them. When the man began to write in mirrored form, a new pattern was probably brought into action, and it seems logical to assume that since this pattern was the mirrored reversal of its predecessor, it was resident in the other cerebral hemisphere. Thus one may envisage the occurrence of the disturbance of speech as due to a conflict between the two hemispheres, comparable to that which frequently occurs when righthanded writing is forced on a lefthanded child. Once the new form of writing was mastered and definitely established in the new direction, the conflict disappeared, and the stuttering also stopped.

SOME OBSERVATIONS ON THE LEUKOCYTE COUNT IN EPILEPSY. HAROLD A. PATTERSON and SAMUEL M. WEINGROW, Arch. Neurol. & Psychiat. **21**:412 (Feb.) 1929.

In a study of 182 cases of epilepsy, 52 per cent of the cases showed leukocytosis, 25.5 per cent gave normal counts, and 20.3 per cent showed leukopenia. The inconstancy of the blood picture in epilepsy, together with the relatively few cases on which the conclusions previously reported are often based, perhaps accounts for the conflict of opinions in the literature. The leukocytosis observed was not neutrophilic but lymphocytic. Definite evidence that epileptic leukocytosis was influenced by digestion was lacking. A remote effect is not produced by either grand or petit mal seizures on the white cell count in idiopathic and nonidiopathic epilepsy. The leukocytosis frequently encountered in epilepsy is not due to the disease itself, but to some concomitant phenomenon. A connection between the leukocyte count in epilepsy and the presence or absence of an aura apparently does not exist. There was no relation between onset and duration and the white cell count in epilepsy. The leukocyte count in epilepsy does not appear to be affected by the secondary anemia which often accompanies this condition.

SANFORD, Chicago.

FACIAL NAEVUS: TUMOR OF THE PONS? ANGIOMA? W. RUSSELL BRAIN, Proc. Roy. Soc. Med. **21**:1319 (June) 1928.

The author reports the case of a tumor of the brain in a girl, aged 11 years. The patient had had a nevus of the face since birth, and for four years before the author saw her had shown the signs and symptoms of a tumor of the brain. The author states that there is a possibility of the tumor being an angioma. He says that Cushing and Lindau have described cases in which angiomas of the brain have been associated with angiomas elsewhere.

WILLIAMSON, New Orleans.

POSTVACCINAL MENINGITIS. A. MORQUIO, Bull. Soc. de pédiat. de Paris **8**:387 (Oct.) 1928.

A girl, aged 8 years, developed the clinical picture of tuberculous meningitis, six days after vaccination. The cerebrospinal fluid contained no tubercle bacilli demonstrable by smear or by inoculation into a guinea-pig, and the tuberculin skin test was negative. The meningitis regressed with the vaccination, and recovery was complete and permanent.

CLAUSEN, Rochester, N. Y.

CRANIAL PERCUSSION. A. F. CANELLI, Nourrisson **16**:313 (Sept.) 1928.

When the cranial bones are affected in such conditions as acquired craniotabes, hydrocephalus, chronic infections and intoxications, it is stated that the primary changes take place in the diploë, causing a thinning of the bone. The author believes that these changes can be detected by light percussion before sufficient softening occurs to give the characteristic sensation obtained by palpation. Corroboration of this primary thinning can be obtained by transillumination.

McCLELLAND, Cleveland.

THE TREATMENT OF MENINGITIS BY THE ENDOPROTEIN OF MENINGOCOCCUS. J. A. CHAVANY, Progrés méd. **1**:9 (Jan. 5) 1929.

Endoprotein is the name given to the product made by boiling and finely dividing cultures of meningococcus grown on ascites gelatin. An isotonic solution is made by adding sterile water to this material. Treatment consists of intraspinal injections of endoprotein combined with intramuscular injections, the amount depending on the number of organisms found in the spinal fluid. Slightly cloudy fluid would receive 1 cc., and purulent fluid would receive 2 cc. A favorable result is indicated by a sharp rise in temperature followed by a diminution of organisms in the spinal fluid. The best results have been obtained in adults. In children, the treatment has been of little benefit.

SANFORD, Chicago.

THE EXAMINATION OF THE MENTAL LEVEL OF THE CHILDREN OF THE TRIBUNAL SCHOOL IN BARCELONA. C. BASSOLS, Soc. Catalana de pediat., Nov. 24, 1927.

Bassols found the Terman modification of the Simon-Binet tests to be more accurate in determining the mental level of school children than the usual method.

SANFORD, Chicago.

A CASE OF CONGENITAL WORDBLINDNESS. M. GUENTHER, Ztschr. f. Kinderforschung **34**:582, 1928.

This case did not show agnosia; the ability to combine symbols and to understand such combinations was disturbed, however.

REICHLE, Cleveland.

THE FIRST APPEARANCE OF REFLEXES IN CHILDREN. M. HAYASHI, J. Pediat. (Tokyo), Dec. 20, 1928, no. 343, p. 2150.

The author examined 428 healthy infants and children with reference to the presence or absence of several of the more important reflexes that are used for diagnostic purposes. His conclusions are: (1) The knee jerk is present almost universally on the first day of life; (2) the achilles tendon reflex becomes more and more frequently positive during the first year but is always obtainable at 2 years of age; (3) the Babinski sign is decidedly present in infants less than 6 months of age, and the normal physiologic limit seems to be at 3 years; (4) the abdominal reflexes gradually develop during the first year and are positive at 2 years of age, and (5) the cremasteric reflex steadily grows positive up to 3 years of age, when it is obtainable in 90 per cent of cases.

KATO, Los Angeles.

Diseases of the Eye

THE EYES OF NURSLINGS. KARL JAROSCHKA, Monatschr. f. Kinderh. **42**:528, 1929.

The author describes crescent-shaped stripes occurring just to the right or left and parallel to the corneoscleral margin. They are particularly marked in the new-born infant and are of a milky color and somewhat elevated. They disappear about the third month and occur in from 70 to 80 per cent of cases. They probably represent the site of muscular attachments.

GERSTLEY, Chicago.

Diseases of the Ear, Nose and Throat

THE DEMONSTRATION OF NONOPAQUE FOREIGN BODIES IN THE ESOPHAGUS. H. G. HEINEKE, Arch. Otolaryng. **8**:718 (Dec.) 1928.

It has been found that in many cases iodized oil 40 per cent is of greater value than barium sulphate in demonstrating foreign bodies in the esophagus. A case is reported in which the foreign body was demonstrated because it had absorbed the iodized oil and had thus become visible.

BARNETT, Chicago.

THE CARE OF CHILDREN'S EARS DURING THE SUMMER. HAROLD HAYES, M. J. & Rec. **128**:341 (Oct. 3) 1928.

Tests made in the public schools of New York and other large cities showed that 14 per cent of the children suffer from a defect of hearing in one ear and that about 6 per cent suffer from deafness in both ears. Many parents are desirous to know how they are to prevent their children from developing ear troubles. Acute conditions of the ear are most prevalent in winter, and these children who have had acute infections in the winter must have special care in the summer. If children are allowed to go in bathing, they should be taught how to blow the nose. The method of blowing the nose is described. Ear trouble in summer is generally due to summer colds or to an infection acquired while bathing. However, the risk of infection in bathing is small.

WILLIAMSON, New Orleans.

LARYNGEAL INTUBATION. MARTIN CALDERIN, Arch. españ. de pediat. **12**:645, 1928.

The author suggests some important modifications in the procedure and particularly in the instrument used. Rigorous asepsis and perfect technic are absolutely necessary.

He suggests the following modification in the instruments: (*a*) A modification in the angle of the obturator, the angle being changed from a rectangle to an obtuse angle, and (*b*) the substitution of tubes with a double bulge in tube and obturator for all procedures of extubation; the tube should be kept permanently threaded. The thread is passed through the nasal orifice and fixed to the ear with adhesive tape. In this way, the thread is not lost, and extraction is always certain and easy.

The author also recommends the employment of tubes smaller than the larynx can take. He uses the small tubes designed by Bayeux.

SCHLUTZ, Minneapolis.

FOREIGN BODIES IN THE TRACHEA AND BRONCHI IN CHILDREN. R. PRIESEL, Ztschr. f. Kinderh. **46**:410 (Sept.) 1928.

An attack of suffocation with cyanosis and a cough resembling that of croup should make a physician think of the possibility of a foreign body in the respiratory passages even when the history is unimportant. Small, smooth, round, foreign bodies like peas, or glass beads, may balance between the glottis and the bifurcation of the trachea and cause a repetition of the initial attack of suffocation from time

to time. On rare occasions, a foreign body lodges in the larynx itself, leading to symptoms of laryngeal stenosis and causing a darkening of both lung fields in the roentgenogram. The possibility must be kept in mind under all circumstances, as is shown by the case of a girl, aged 10 years, with progressive bulbar paralysis, who became suddenly blue and threatened to choke while eating a frankfurter; also by a boy, aged 5 years, with diabetes, who was being treated for hypoglycemia with orange juice when he began to struggle for the want of air because of the lodging of a segment of orange in the entrance to the larynx. Roentgen examination will help to tell whether a piece of foreign body has been left after extraction of apparently the whole object. It is important to obtain a roentgenogram early because a quick extraction is the only way to prevent pneumonia.

EMERSON, Boston.

Diseases of the Skin

PEMPHIGUS HEREDITARIUS. KARL H. KUSE, Monatschr. f. Kinderh. **42**:513, 1929.

In 1922, Mautner described a type of pemphigus in the new-born infant differing from both the congenital and the acquired types and characterized by its familial nature and fatal ending. The author reports a case and reviews the literature. His conclusions are that it is unquestionably an hereditary disease. Both sexes are equally involved, and the disease starts soon after birth. The whole body is affected, with a tendency to ulceration and destruction of bone, cartilage and nails. The vesicles do not result from mechanical irritation nor are the mucous membranes invariably concerned. Bacteriologic examination of the vesicle content shows no typical organism. There is no known treatment.

GERSTLEY, Chicago.

THE PATHOGENESIS OF SUBCUTANEOUS FAT NECROSES OF THE NEWLY BORN (SO-CALLED SCLERODERMA NEONATORUM) FROM THE POINT OF VIEW OF A REACTION TO COLD ON THE PART OF THE SUBCUTANEOUS ADIPOSE TISSUE IN NEWLY BORN AND YOUNG INFANTS: II. LEO LEMEZ, Ztschr. f. Kinderh. **46**:323 (Sept.) 1928.

By the influence of cold (a spray of ethyl chloride for from thirty to fifty seconds or by the application of ice) one can cause in newly born and young infants a hardening of the fat tissue, analogous clinically to the necrosis of fatty tissue. The infiltration provoked under the skin is of the consistency of rubber; it is sharply outlined and capable of being grasped, and the overlying skin is red to bluish red or shows an increased dermographism. As to the intensity and duration of the infiltration, four grades can be distinguished. This reaction of the fatty tissue to artificial cold depends on the chemical composition of the fat underlying the skin, the intensity of the cold, the quantity of the subcutaneous fatty tissue and the susceptibility of the organism to inflammation. The reaction of adipose tissue to cold sometimes remains latent for a long time. It is a specific biologic latency in the fetal fat of the newly born infant, and the maturing process of the fetal fat and the diminution of the reaction to cold go hand in hand. This reaction and the necrosis of fatty tissue are identical with regard to the disease picture, the clinical course and the conditions necessary for their occurrence.

The view of Cruse that extreme cooling of the skin may cause a hardening of the fatty tissue is confirmed. Trauma and cold in the skin of the newly born infant influence one another in the sense of an increase of reaction, and the clinical evidence which Bernheim-Karrer and Heidler have brought forward, that trauma is an etiologic agent, is confirmed. Severe injury of the subcutaneous fat by heat hinders the reaction to cold. The only injury to the fatty tissue that can cause its hardening clinically is that which vitally harms the fat cells so that death of the cell occurs while the content, the fat, is left intact.

In three cases of necrosis of the fat in the new-born, it was found that the first stages appearing in the skin stayed the longest. In one case, it was established from the history and in another by clinical observation that there was a preliminary edematous stage. The infiltration of fatty tissue can be increased in the stage of formation but not in that of retrogression. The histologic data in the first case at the thirty-fifth day of life corresponded to those of a much older stage of the disease at the seventieth day of life. It appears that next to the duration of the condition, its latency influences the histologic picture. The first and third cases demonstrated a dependence of the fatty necroses on the previous trauma, and in the second case this condition was probable. Treatments with cold water at birth in the first and third cases were considered as supporting agents for the origin of the condition. On the basis of their own experiments, however, trauma was recognized by the authors as a source of the condition, in agreement with the great majority of workers, the action of cold as an etiologic agent being discovered only occasionally. During the first months after birth, subcutaneous fat, like fetal fat, is still being formed, but after the fourth or fifth month of life, positive reactions of fatty tissue to cold are to be looked on as an anomaly in the formation of fat.

EMERSON, Boston.

Surgery and Orthopedics

CONGENITAL HYDRONEPHROSIS IN AN INFANT OF SEVEN MONTHS; NEPHRECTOMY; CURE. A. MARTIN, Bull. Soc. de pédiat. de Paris **8**:386 (Oct.) 1928.

Martin presents an interesting case report.

PALLOR WITH HYPERTHERMIA IN AN INFANT AFTER OPERATION; RECOVERY. J. ARMINGEAT, Bull. Soc. de pédiat. de Paris **8**:422 (Oct.) 1928.

After an extensive operation, an infant, aged 9 months, developed high fever, pallor, a low alkali reserve and a low blood pressure. In spite of obvious dehydration, no mention is made of injections of fluid. Epinephrine, digitalis and cold spongings were used.

CLAUSEN, Rochester, N. Y.

Miscellaneous

THE REACTION OF THE PLEURA AND LUNGS TO ROENTGEN RAYS. ARTHUR U. DESJARDINS, Am. J. Roentgenol. **16**:444 (Nov.) 1926.

The author states that pulmonary fibrosis may be the final phase of the reaction, but the usual temporary reaction is a pleuropneumonitis, which usually appears in from two to four weeks after roentgen treatment. The symptoms usually are cough, shortness of breath and sometimes fever. Physical signs are usually limited to one side and depend on the degree, extent and situation of the pleural or pulmonary tissue injured. Roentgen study may show merely a diffuse fog of inflammatory pleural thickening, with or without the denser shadow of effusion, or it may simulate the focal type of pneumonia or pulmonary abscess. Differential diagnosis includes metastatic neoplasms, abscess of the lung and other inflammatory reactions. Apparently the short wave length is not as potent a factor in the reaction as is the quantitative factor represented by the distance and duration of exposure.

STULIK, Chicago

DISEASES OF THE CHEST DEMONSTRATED BY LIPIODOL. A. HOWARD PIRIE, Am. J. Roentgenol. **16**:553 (Dec.) 1926.

The injection of iodized oil 40 per cent produces a characteristic picture in bronchiectasis through filling of the proximal parts of the dilated bronchioles. The oil, however, will not run into the alveoli or through openings smaller than 3 mm. in size. It will not enter an abscess, if the abscess is full of pus, or if it is above the level of the injection. Stenosis of the trachea and bronchi is readily

visualized. Other indications for visualization by means of iodized oil are: suspected bronchiectasis; suspected tuberculosis when tubercle bacilli cannot be found in the sputum; unfavorable condition of the patient after thoracoplasty; for demarcation of the diaphragm when it is invisible in subdiaphragmatic abscess; for exclusion of bronchiectasis before thoracoplasty is done; for stenosis; for demonstration of a tuberculous cavity; for bronchopleural fistula; for foreign bodies, and for the negative diagnosis of bronchiectasis.

A Study of the Relationship Between Type of Ventilation and Respiratory Illness in Certain Schools of New Haven, Conn. L. Greenburg, Pub. Health Rep. **44**:285 (Feb. 8) 1929.

Two groups of 1,500 children were studied. One group attended schools ventilated by mechanical means, and the other went to schools employing the natural method of open windows. The total data concerning absence caused by diseases of the respiratory tract show 3.0 per cent for the group subjected to mechanical ventilation, and 1.8 per cent for the group in the school with natural ventilation.

Sanford, Chicago.

Some Medical Emergencies in Childhood. I. C. Spence, Practitioner **121**:384 (Dec.) 1928.

Hemorrhagic disease of the new-born infant is serious and often fatal. Prompt remedial measures are necessary. The treatment is the intramuscular injection of whole blood of either parent, preferably the mother. This appears to supply some factor lacking in the infant's blood which stops the bleeding. An injection of 10 or 20 cc. should be made three times on the first day, twice on the second day and once on the third day. When the bleeding has been stopped for two or three days, the cure is permanent, probably because by that time the infant's own tissues become capable of providing the hemostatic factor.

In vomiting caused by hypertrophic pyloric stenosis, it is a matter of prime importance to make the diagnosis as quickly as possible. Then the mother must be persuaded to continue to feed the child at the breast or to restore it to the breast if it has already been weaned.

Whatever the ultimate details of treatment, the most important point is that the child be breast fed. The mortality rate in breast-fed infants should be less than 10 per cent. In artificially fed children, it approaches 50 per cent.

In diarrhea the great danger and emergency arise not so much from the original infection as from the state of dehydration which the diarrhea causes. Both water and essential mineral matter are lost from the blood and tissue fluids. The blood is diminished in volume, and a condition of acidosis results from diminished oxidation.

It is important to prevent these symptoms by replacing the fluids lost. Ringer's solution, half strength physiologic solution of sodium chloride or Vichy water may be used; the latter supplies some of the mineral matter.

When dehydration has already occurred, subcutaneous and intraperitoneal injection of Ringer's solution, physiologic solution of sodium chloride and dextrose should be used.

When an infant is born in a household in which tuberculosis is present the great danger is in the first few weeks, when there is no resistance against the infection. Resistance increases as the age increases so that a child aged 3 years will withstand an infection which would cause a serious disease in an infant aged 3 weeks.

The infective person is often not a parent. A maid, nurse or regular visitor may be the source of infection.

A child born in a household in which some one is known to have an active infection should be immediately removed from the source of infection.

Paul S. Barrett, San Francisco.

Society Transactions

PHILADELPHIA PEDIATRIC SOCIETY

Stated Meeting, Nov. 13, 1928

EDWARD L. BAUER, M.D., *President, in the Chair*

VACCINATION AGAINST THE COMMON COLD. DR. J. A. KOLMER.

The nasal mucosa is subject to a wide variety of influences resulting in the production of congestion and discharge. Temporary congestion, sneezing and discharge due to sudden exposure to heat, cold and drafts may not necessarily be a "common cold." Of course, the same is true of the congestion and discharge due to allergic conditions, notably in hay-fever and the so-called "vasomotor rhinitis."

The term "common cold" should be reserved for the designation of those cases usually traceable to contact with other cases and beginning malaise, dryness of the nose and throat and itchiness followed by profuse excoriating nasal secretions which in a few days become scanty and mucopurulent.

The etiology of the "common cold" is as yet an unsolved problem. It may be that aerobic organisms easily cultivable from the mucopurulent discharges of the common cold are the etiologic agents, especially staphylococci, *M. catarrhalis*, pneumococci, streptococci, etc. At least, organisms of this group are usually responsible for such complications as parasinusitis and bronchitis.

Some investigators regard the etiologic agent as a filtrable virus. This claim was first advanced by Kruse in 1914, and by Foster in 1917. The evidence, however, is not clear and has been disputed by several investigators.

It cannot be said that the common cold has been produced by installation into the normal nose of staphylococci, *M. catarrhalis*, pneumococci, streptococci or other organisms; as a matter of fact, the installation of such organisms is followed by their rapid disappearance, as shown by Bloomfield. Nor can it be stated that the gram-negative, filter-passing, anaerobic bacteria bear an etiologic relationship to the disease.

Vaccination has been attempted with mixed stock or autogenous vaccines of the aerobic organisms previously mentioned. Stock vaccines may be first tried and if found ineffective should be followed by the careful preparation of an autogenous vaccine prepared of organisms recovered in cultures during the purulent stage of the disease. It is probably good practice to use a mixed stock and autogenous vaccine.

The vaccine may contain a total of 1,000,000,000 per cubic centimeter. An adult may receive 0.5 cc. for the first dose followed by three subsequent doses of 1 cc. each at weekly intervals. Children may receive one-half these amounts.

Patients for vaccination should be carefully selected, and only those found free from polyps, anatomic defects, etc., should be regarded as suitable subjects.

Immunity is apparently produced in about 60 per cent of persons. This immunity is usually of short duration. When vaccination is practiced in October, the disease may recur in the early spring months, although in many instances the immunity has been observed to persist for from one to two years.

In the case of persons suffering with frequent attacks of common cold, Dr. Kolmer regards vaccination as distinctly worth while. Even though the disease may not be entirely prevented, it is frequently observed that subsequent attacks are mild and of brief duration.

Vaccination plus hygienic precautions have given particularly encouraging results.

DISCUSSION

DR. J. C. GITTINGS: Until the bacteriologists tell us exactly what causes colds and exactly what will happen in the patient when we inject a few million

bacteria, it seems to be inevitable that we shall indulge in that dangerous pastime of drawing conclusions from our personal experiences. Such conclusions are never safe except when based on several thousand experiences. Nevertheless, there seems to be nothing else for us to do. My own experience in the use of vaccines for the prevention of colds is about the same as that of Dr. Kolmer: In selected cases, those without definite pathologic changes, in patients who give a history of having had serious colds which they had great difficult in getting over and which have been apt to lead to complications, I have found that a considerable percentage, I should say roughly 50 per cent, have succeeded in going through the winter without a cold or without serious colds; however, some may have slight colds. I have had the experience that some particularly susceptible persons do well until March and then contract a cold; in these cases, I give repeated inoculation around the first of February, and in a fair percentage of them obtain good results. I have felt that my results are better if the patient, after the second or third inoculation, has some symptoms of cold, sneezing, a feeling of some fulness of the nose and sometimes even a slight rise in temperature. It is hard to believe that these symptoms are entirely without significance.

It makes one feel somewhat more inclined to give vaccines for cold.

I had one curious experience in a boy, aged 8 or 9, who had a severe cold, whom I inoculated successfully for two years. In the fall of 1927 I gave him his usual inoculation, but I increased the dose. With several of his severe colds before this he had pronounced bradycardia, his pulse rate decreased in the night to 40 or 45 and he woke up in a severe sweat. During inoculations he was free from cold and had mild attacks of sinus bradycardia, which were not so severe. The psychic effect Dr. Kolmer mentions he sees, I suppose, more in evidence in adults. It is hard to believe that children, except the very precocious, around the ages of 8 or 10, would have psychic effect, but I am inclined to believe that the psychic effect is exerted on the mother. It is possible to believe that the cold the child gets after receiving vaccine is not so severe as before. I have used stock vaccines on the theory that they include the ordinary organisms of cold. In the first place, if one makes an autogenous vaccine in any given case, one has to wait until the patients have a cold in order to obtain a good one. In the second place, are we sure that the same organisms are always involved? It is possible that the predominating type in one case may not be that in another. If one makes autogenous vaccine, it is barely possible that one may not protect the person later in the year. Results are better with stock than with autogenous vaccines.

Dr. G. B. Wood: I have had the opportunity, which is one of the happy experiences of my life, of being more or less closely associated with Dr. Kolmer. I have asked him numerous questions about colds, and my ignorance of bacteriology perhaps is the reason I want to ask him one more question.

In a case of acute rhinitis, as I understand the disease, the condition clears up because of the immunity produced by the organism which produces the disease. Why does not this immunity protect against another cold as does the injection of some organisms after they are killed?

There may be some good bacteriologic explanation of that fact. If we consider scarlet fever we know that when patients recover from that disease, they became permanently immune. Of course, one does not have permanent immunity from cold. Why does not one become immune to common cold as one does when dead organisms are introduced?

Dr. Percival Nicholson, Ardmore, Pa.: If vaccine is given for protection one winter and then repeated the next winter and again the third winter, is there any evidence to show that the patient tends to show permanent immunity to the renewal of the same type of infection? In small parts of the world, infections occur, and after a time the people obtain more or less permanent immunity. Is it fairly good judgment to use stock vaccine in cold, and after that fails in the course of two or three months if the patient develops cold at that time and is given an autogenous vaccine, is there more likelihood of getting an overgrowth of a large number of organisms originally present?

DR. THOMAS BUTLER, Bethlehem, Pa.: In whooping cough in children aged 1 year, which we all regard with such fear, I have seen marvelous results following the injection of diphtheria antitoxin. I should like an explanation from Dr. Kolmer as to how these results may be accounted for.

DR. J. A. KOLMER: The question of Dr. Wood is logical and not easy of reply, namely, why should we expect immunity from vaccine if an immunity fails to develop after an attack or repeated attacks of the disease? I can answer this question only in the light of our present knowledge by stating that the duration of the ordinary attack of common cold is too brief for the protection of immunity. If *Staphylococcus albus, Micrococcus catarrhalis,* pneumococci and streptococci are real etiologic agents, we must assume from the outset that immunity to them develops rather slowly. That is one reason that active immunization against scarlet fever has not fulfilled the original expectations, because the human body reacts rather slowly to the pathogenic cocci, with the production of immunity principles. It is likewise one reason that a patient going through an attack of diphtheria may fail to develop a subsequent immunity to the disease, because since the introduction of antitoxin in treatment the infection is cut short too quickly for this rather slowly acting immunization mechanism of the human body. I do not doubt that we are going to see many more cases of secondary scarlet fever in the future for exactly the same reason, since we may, by cutting short the attack of scarlet fever, rob the patient of the more or less permanent immunity that would have been his had we allowed him to go through the usual course of the disease.

In reply to the question of Dr. Nicholson, so far as my impressions are concerned, we have little reason at present for expecting a durable immunity from a single vaccination. My experience has been fairly similar to that of Dr. Gitting in that the immunity must be measured in months rather than in years, although there are some who have gone through two years of freedom from colds and are now approaching their third year.

I regard the suggestion and practice of Dr. Nicholson of starting with stock vaccines as excellent.

In reply to Dr. Butler, I have had no experience with the influence of diphtheria antitoxin in the treatment for or the prevention of the "common cold." The results reported from the use of diphtheria antitoxin in whooping cough may have been due to what is commonly designated as nonspecific protein reaction. We now realize that a nonspecific protein reaction may have a prophylactic as well as a curative effect, and it may be that in some cases a serum may result in a certain degree of protection to the "common cold."

THE PREVENTION AND TREATMENT OF COMMON COLDS IN CHILDREN. DR. W. B. DAVIS.

The "common cold" is a transmissible mixed infection, for which no specific causative micro-organism has as yet been demonstrated. In children colds assume greater importance than in later life, since a larger percentage have extension to the middle ear, mastoid cells, nasal sinuses and lower respiratory tract.

In the prevention of colds we must emphasize the importance of maintaining good health and resistance. Attention should be given to proper diet, out-door life, exercise, proper bathing, regulation of ventilation and heating, adjustment of clothing to climatic conditions and avoidance of undue exposure, especially when overheated or tired.

The local conditions which predispose a child to colds are:

1. Some focus of subacute or chronic infection in the pharyngeal, nasal or paranasal areas, most frequently found in the tonsils and adenoids, by no means infrequently present in the paranasal sinuses, or in the small lymphoid follicles on the posterior pharyngeal wall.

2. Obstructions which interfere with free nasal respiration and the ventilation and drainage of the nasal accessory sinuses. The obstructions by far most fre-

quently observed in children are enlarged tonsils and adenoids. Less frequently seen are hypertrophied turbinates, deflections of the nasal septum, septal ridges and spurs, nasal polypi, mucous cysts, foreign bodies and nasal and pharyngeal tumors.

Local prophylaxis consists in clearing up the infections. Nasal surgery in children, however, calls for conservative judgment, accurate anatomic knowledge and refined technic. The removal of the enlarged and the chronically infected tonsils and adenoids is beneficial in a large percentage of cases. In the vast majority of cases, not only fewer colds are contracted, but those which do occur clear up in shorter time, and complications are much less frequent.

Sinus infections clear up with less difficulty after tonsillectomy, and when infection persists both local measures and vaccines are necessary. I believe that vaccine therapy is of greater value in clearing up infections in sinuses than it is in establishing immunity to colds.

A general plan of treatment for colds in children might be outlined as follows:

1. The early administration of a laxative.

2. A hot mustard foot-bath followed by rest in bed for one or two days. This isolation is also a prophylactic measure, since the child is thus kept away from playmates.

3. A light diet and an abundance of water.

4. Atropine sulphate in small doses, at from three to six-hour intervals.

5. The internal administration of sodium bicarbonate, or some other alkalinizing agent. Small doses of some salicylate may be combined with the soda with benefit.

6. The use of mineral oil with a medicine dropper every three hours. Every six hours, following the mineral oil, several drops of 10 per cent mild silver protein solution should be used.

7. Instead of plain mineral oil the use of a prescription containing 1 grain (0.065 Gm.) of menthol, or else 1 grain (0.065 Gm.) of camphor, to 1 ounce (30 cc.) of mineral oil tends to decrease the congestion. I believe stronger solutions than this are too irritating.

8. Solutions of epinephrine and similar preparations quickly relieve congestion, but the reactionary congestion which follows is so much greater than the original conditions that I regard their use as inadvisable.

9. Nasal applications of ephedrine solutions are also followed by secondary local reactions but not so marked as those which follow the use of epinephrine.

10. When the congestion is fairly marked, I prefer the use, every six hours, of from 2 to 5 drops of a prescription containing 1 grain (0.065 Gm.) of cocaine alkaloid, 1 grain of camphor, 1 drop of oil of cinnamon, to an ounce of liquid petrolatum. This gives great relief and is seldom followed by reactionary congestion.

11. The use of camphor-ice about the anterior nares minimizes the irritating effect of the nasal secretion on the surrounding skin.

12. Warm salt solution or an alkaline gargle several times a day is advisable in older children. Applications of mercurochrome-220 soluble (from 2 to 5 per cent solutions) to the posterior and lateral pharyngeal walls are often beneficial. In the last two decades much progress has been made in the prevention of and the treatment for colds in children, but it is still a field which demands further improvement.

DISCUSSION

DR. BABBITT: A discussion of this finished paper of Dr. Davis is the more difficult because one agrees so perfectly with the matter he has read. I should be inclined to place special emphasis on the preventive value in the removal of adenoids. The otolaryngologist usually sees the patient who has frequent colds in the interim period, while the family physician or pediatrician usually sees them in the acute stages and observes their recovery. He, therefore, may have

a great deal of information about these patients which will tell us what operative measures may be expected to accomplish.

I think we are coming to believe that the common cold must often be considered as an upper respiratory expression of disordered metabolism aided by existing foci of trouble. It is discouraging to note how often the household observing good hygiene and giving constant attention to colds may seem to be constantly subject to them, while the members of another family will have no colds despite every carelessness and neglect. No matter what is done for some persons with recurrent colds, they keep on having them. In evaluating therapeutic measures, it must be remembered that occasionally colds get better themselves. Experience has proved that active local treatments may as often irritate and prolong the common cold as relieve it; therefore, this may well be essentially one for pediatric care.

DR. W. B. DAVIS: The fact that one household has colds and the neighbors have none is commonly called to the attention of physicians. I believe there is a distinct hereditary tendency to colds. Observation of the structure of the noses of a family often shows similar anatomic peculiarities in parent and child and in sister and brother.

WHY COLDS? DR. J. H. MCKEE.

There is no reasonable excuse for calling respiratory infections "colds." We call them colds, but every one knows they are infections. If people talk in terms of cold, they think in terms of cold and the mother's history of the infant's illness stresses "the exposure after his bath," "the cold wind that came up during the night," "the baby's escape from the bed-clothes," or "the draft from that open window" in a vain search for a cause. She misses the real preventive measures, the asepsis and antisepsis in the treatment of the sick and the prevention of spread to others.

To do justice to the infectious demonstration made long ago, one should also mention the classic contributions of Curtin and Watson to the Climatologist during the early nineties. Curtin himself was a veritable mark for these infections; he spoke of his personal susceptibility as his pathognomonic sign in diagnosis. Sir William Osler, too, had his usefulness handicapped and his splendid health marred by repeated "schnupfens," and the Pfeiffer bacillus caused the low-grade pneumonia and the pleural effusion that ended his illustrious days.

The diagnosis of grip or influenza is often made too loosely. In view of Welt-Kakel's bacteriologic studies for Dr. Holt and in virtue of the difficulties encountered in isolating the Pfeiffer bacillus in the upper air passages and also in the lower respiratory tract after mixed infections have occurred, I am inclined to think that the balance of error is probably on the other side. We must recognize the important etiologic rôles played by pneumococci, Friedlander bacillus, *Micrococcus catarrhalis*, diphtheroids and the various pus-forming organisms. Now we must add *Bacillus bronchisepticus* to the list.

At Camp Lee during the autumn of 1918, two negro regiments of the same fighting strength were encamped side by side. Nothing had seemed to have a deterring influence on the spread of the devastating "flu" epidemic of that year. Despite the protests of Victor Vaughan, unnecessary traveling and troop movements went on all over the land. One of the negro regiments was given the following order: "Wash your mess-kits with as hot water as you can secure from the field kitchen, and dry them with sterile dish-towels." To Regiment *B*, a different instruction was issued: "Boil your mess-kits and drain them dry." From then on, the daily incidence of influenza was from two to four times as great in Regiment *A* as that in Regiment *B*. Hand infection is probably the largest factor in the transmission of respiratory infections. In the Infant and Child's Hospital at Harvard, when the rule was formulated that no physician or nurse should pass from one child's bed to another without washing the hands, crossed infections fell from 16 to 6 per cent.

Probably there is no more dangerous contaminator of human hands than the soiled handkerchief. The clean handkerchief is never clean after it has once been used.

Toys, passed from hand to hand, come under the same category as handkerchiefs. So do lead pencils. Dishes may be infected by members of the household. Their care cannot be too sanitary.

Children may be infected while swimming, not only in pools, but also in rivers, bays and other waters environing a great city. In waters about New York were found the various organisms concerned in the production of disease of the eye, infections of the nose and throat, diseases of the middle ear and mastoiditis. The swimmers thought they had taken cold lolling about in wet bathing suits, when as a matter of fact they had been infected by the waters.

Is the infectious element the only one in the causation of the conditions under discussion? Animal emanations, plant pollens, street and house dust, certain foodstuffs and countless other things may irritate the mucous membranes of sensitive subjects. However, even in the presence of such demonstrable conditions, bacteria may come to play important rôles.

I do not deny the influence of cold. The child with wet feet, with clothing drenched or chilled to the marrow because of insufficient clothing, may readily have his resistance lowered to the danger point. Often, the traditional cart is placed before the horse: "As soon as that draft struck me I began to sneeze." While admitting the depressing effects of bodily chilling, one must hasten to say that there are countless other factors in our lives that may have as great, or possibly greater, influences in reducing bodily resistance than out-of-door cold or God-given drafts of fresh air: undernourishment, overeating, disturbed digestion, bodily fatigue, too warm clothing and most of all overheating of houses or the dry heat of the steam or hot water heated apartment, school, office building, church or hall. Persons tend to remain indoors more and more; in stuffy, overheated rooms, they come into closer relationship with more of their kind and therefore with more infections.

Certain people are exceedingly sensitive to weather changes and draught. I know of no such selfishness in life as the supreme selfishness of the man who would have hundreds, perhaps thousands, of his fellows suffer, because he chances to feel the draft of air in church, hall, theater or public vehicle. One is tempted to say that the people who are sensitive to drafts are the very people who ought to sit in them; the people who by the use of lighter clothing and daily cold showers ought to harden themselves for their own good and the comfort of their associates.

One cannot dismiss this subject of etiology without stressing the importance of tissues of lessened resistance, for such areas invite respiratory infection. The tissues comprising the Waldeyer ring take the place of foremost importance. Diseased tonsils, like diseased appendixes, are menaces to the lives and health of their possessors. I have never seen a healthy tonsil removed at operation. In the presence of heart disease, only dangerous decompensation would lead me to defer the procedure that might save the heart.

There are other tissues minoris resistentiae, the badly deflected septum and the infected sinuses. I believe that pediatricians view the tonsillar histories in the making for months or years after tonsillectomies, and that the opportunities are theirs to note the successes or failures of operations.

Hyperplastic tracheobronchial glands may render their possessors extremely sensitive to bronchial infections.

Should we not throw the term cold into the verbal discard, and speak of nasal infection, throat infection, laryngitis, tracheitis and bronchitis, as the case may be?

Knowledge and propagandism are the two effective agents in compassing any true reform. When with the same energy and the same coordination they are directed against the respiratory infections as they were against the summer diarrheas, similar results may be anticipated.

To obtain effective prophylaxis personal responsibility must be made clear to every intelligent adult. If he contracts a respiratory infection, he should isolate

himself from his family, friends and business associates. This need not be a literal isolation, but it should be a hygienic one. Toward infants and little children his responsibility is probably greatest of all. In the experience of all of us, some infant has suffered severe illness or even death because some ignorant or careless adult has unwittingly carried such an infection to him. Careful cleansing of his hands, the use of gauze or paper handkerchiefs for nasal and bronchial secretion, the subsequent boiling and draining of eating and drinking utensils are not so much to impose on him.

Clear views of the matter and aroused consciences will keep one from sending children so infected to school or Sunday school. Teachers could help a great deal in this matter; however, they often fear to have attendance rolls cut down. I hope to see the day when every child with an acute coryza or a cough will be sent from school. If a few are so sent in the early days of an epidemic, there will be fewer to send later on.

After the postnatal period, babies should gradually be acclimated to the great outdoors. Usually if one advocates that a baby be kept out a certain number of hours, it will be found that the actual time is much less. Outdoors all day is none too much, rain or snow alone leading to the reproduction of outdoor conditions in the room or sleeping porch. The artificial heat of houses particularly intensely dry heat, is far more dangerous than the cold air of the open.

So, in general, is overdressing more dangerous than underdressing. The baby should be dressed for the house as for a summer day with a temperature of 70 F. warm outer garments should be depended on for outdoor wear.

If children are particularly sensitive to cold air or to cold water, they should gradually be accustomed to lighter clothing and to cooler bathing.

The treatment of the sick patient is another story, and of course it cannot be adequately covered here, but I find it impossible to close without a few aphorisms that have meant much to me:

1. The sick baby or child is best at rest.

2. His room should be well ventilated, and kept at an even temperature (68. F.).

3. Most respiratory infections begin in the nose. It becomes our duty to keep them there or to abort them before they pass further down.

4. Belladonna and atropine are useful for accomplishing the last named object. They dry up secretion and stimulate respiration, circulation and thermogenesis.

5. The late Dr. Walter Freeman and the late Dr. Hitschler taught me to douche the nose properly. Dr. Hitschler "scotched" the common belief that douching causes disease of the middle ear. Of 400 cases of diphtheria and scarlet fever at the Municipal Hospital, 200 were douched and 200 were not. The number of ear complications was the same in the two series. Such cleansing is followed by the use of some good solution of liquid petrolatum, and weak ephedrine solutions in liquid petrolatum have served well.

Respiratory infections tend to run rather definite and prolonged courses when once intrenched in the human organism. While making rounds at the Germantown Hospital last winter, a noted French clinician made the following remark, "If you don't treat a cold, it runs for three weeks. If you do treat it, it lasts twenty-one days."

DISCUSSION

DR. G. B. WOOD: There is no doubt that if we could teach every one, including parents, school teachers and other public officials, that the so-called common cold is the result of contagion, physicians would see fewer patients. It must be admitted, however, that the etiology of these infections is still obscure. As to the various so-called predisposing factors, an interesting study was made two or three years ago covering large numbers of persons of all classes of life. It was shown that there was practically no single factor of life habit that had any influence on the incidence of infection, except that those who slept in hot unventilated rooms had a greater percentage of colds than any one else.

If one is careful to avoid contamination from the nostrils in making nasal cultures it would be found that the interior of the normal nose is practically sterile.

Bloomfield of Johns Hopkins, a few years ago, showed that practically all types of bacteria when introduced inside of the nasal cavity are rapidly removed; this work has just been substantiated by Arnold, Strom and Singer. The latter also showed that there was a definite ratio of disappearance of these organisms from the nose and that this disappearance was not affected by cold, drafts, etc. On the other hand, a hot room did produce a distinct lessening of the rapidity with which these organisms were removed.

If we are to have a temperature nomenclature for diseases it would seem that the term "common hot" would be much more exact than "common cold" as a designation for acute infections of the upper respiratory tract.

DR. E. L. BAUER: Dr. Hitschler's technic of nasal douching must have become a lost art at the Municipal Hospital. When the practice was abandoned at the suggestion of Dr. C. W. Schaeffer, fifteen years ago, the incidence of ear complications was remarkably reduced in cases of scarlet fever. It has never returned to the level prevailing when nasal douching was the vogue.

CHICAGO PEDIATRIC SOCIETY

Regular Meeting, Jan. 15, 1929

M. L. BLATT, M.D., *President, Presiding*

HYPOSUPRARENALISM. DR. M. G. PETERMAN, Milwaukee.

The report of this case was published in full in this journal.

DISCUSSION

DR. ISAAC A. ABT: We know a great deal about the pharmacology of the suprarenal gland when it is administered hypodermically, or applied locally, but our knowledge remains limited regarding the precise function or the pathologic conditions of the gland. I think we know little more than was known when Addison described his famous disease. I recall that in Lesage's book on diseases of the new-born he speaks of hyposuprarenalism, and says that this condition in young infants may easily simulate a meningitis. Those of us who have seen severe hemorrhage into the suprarenal glands in new-born infants will remember how often the differential diagnosis is impossible, or is confused with meningitis.

DR. M. G. PETERMAN: I regret that it was impossible to secure a complete necropsy, so that we might have searched for enlarged glands or for the thymus. The patient was brought in at about 5 p. m. on Saturday and died at 6 p. m. on Sunday; so we had only a limited time. I regret that there was not sufficient time for better study of his response to epinephrine. There was no general enlargement of the glands, and clinically no enlargement of the thymus, which does not mean that it was not enlarged. Because of the necessary limitation of the necropsy I do not know whether there was any other pathologic process present, but with the bronzed skin, the low blood sugar and the other symptoms described, we made a diagnosis of hyposuprarenalism, and all the suprarenal tissue we could find was that shown in the slides.

CLINICAL AND SURGICAL OBSERVATIONS OF ACUTE APPENDICITIS IN CHILDREN. DR. BERNARD PORTIS, Chicago.

Eighty-five consecutive appendectomies performed by the author from his private practice and ward service at the Michael Reese Hospital are included in this report. These cases represent practically all the common forms of pathologic conditions of the appendix which are shown by patients on entrance to a large charity hospital. In many of the patients the condition has been neglected, and the patient is seen late after the onset and, frequently, after having been subjected to drastic purging. There were only three deaths in children who had overwhelming peritoneal inflammation.

The rotation of the cecum during embryonic development with the anatomic and histologic features of the appendix is next considered, demonstrating, first, the various locations the appendix may assume; and, second, the richness of the lymphoid elements and tendency of the edema of the organ to produce anemic infarction. These are the essential factors which lead to the frequently and progressive character of the acute inflammatory conditions of the appendix.

The special clinical features considered are: 1. Pain was generalized in 75 per cent of the patients and localized after a variable period to the right lower quadrant. 2. There was the constant presence of some form of gastro-intestinal distress. 3. The temperature was increased, and in four cases there was a rapid rise with persistently low leukocyte count associated with gangrene of the appendix. The leukocyte count was increased, but the degree could not serve as a reliable operative index. Localized tenderness over the lower right quadrant was the most important physical observation, while rigidity was indefinite in the early stages of appendicitis.

Even after careful consideration of the symptomatology and physical symptoms, there are still numerous obstacles in arriving at a correct diagnosis and in determining whether or not surgical intervention should be undertaken. In many borderline cases the diagnosis is made only after exclusion of such conditions as acute pyelitis, gastro-enteritic infections of the upper respiratory tract, mesenteric lymphadenitis, intussusception, pneumococcic peritonitis and any of the many causes of acute conditions of the abdomen in adults which require surgical intervention.

The dictum followed by the author is that once the diagnosis of acute appendicitis is made, operation should be performed without delay, and the appendix should be removed in all cases in which it is humanly possible without subjecting the patient to too great a risk. The possible complications from simple drainage of an appendiceal abscess without removing the appendix are then considered. Absolute rest and frequent gastric lavage with fluids by hypodermoclysis, or intravenously, during the first few days of paralytic ileus was found advantageous in comparison to other methods of treatment. Blood transfusion by the direct method is a valuable aid when the patient is in a toxic and critical condition.

In conclusion, the author makes a plea for close cooperation between the pediatrician and the surgeon, and in doubtful cases, with many symptoms consistent with acute appendicitis, operation should be performed and done, if need be, under local anesthetic.

DISCUSSION

Dr. Joseph Brennemann: Dr. Portis has given us a complete and lucid statement concerning the complex problem of appendicitis. There are one or two points that I would like to stress. The first of these is the paramount significance of a point of tenderness on the right side of the abdomen, usually in the lower right quadrant, but not always. The pain is usually first about the umbilicus and later may not be sharply located, but the tenderness is always over the point involved. This alone will usually be able to exclude the pain and tenderness in the abdomen which is so common an accompaniment of pneumonia, pleurisy, pericarditis and infections of the upper respiratory tract. Even in the presence of any of these things it must always be remembered that there may be a coincidental or accompanying appendicitis, and the diagnosis of the latter should be made regardless of the other conditions, if there is a definite, localized point of tenderness, and especially, but not necessarily, if there is at the same time an involuntary rigidity.

The second point that I would stress is that even if there is pyuria or a hematuria this would not in any way tend to exclude the diagnosis of appendicitis, if the symptoms pointed definitely toward that condition.

DISCUSSION

Dr. Julius H. Hess: Dr. Portis made the statement that a child with pain in the abdomen has appendicitis until this diagnosis is ruled out. Dr. Brennemann said the surgeon does not see the cases from the same standpoint that we do,

but the more I see of these conditions of the abdomen in children from 1 or 2 up to 8 years of age, seemingly the less I know about them.

Almost everything that has been said has been centered around the acute condition within the appendix, and I wish to refer briefly to a few cases in which the patients have come to us with a diagnosis of appendicitis in which a differential diagnosis was obligatory.

The first case was that of a boy, aged 8, who had had repeated attacks of more or less generalized pain in the abdomen. When I first saw him five weeks ago in the midst of one of these attacks, there was complete absence of localization. That attack passed and three weeks later I saw him again, when the condition was well centered over McBurney's point. He was sent into the hospital and operated on, a simple catarrhal appendix being removed. The surgeon was not satisfied that this type of appendix accounted for the repeated attack of pain over several years and the recent history of the case, and on further search about 5 inches (12.70 cm.) above the ileocecal junction he found a band which caused a half twist in the ileum with almost complete obstruction. This had undoubtedly caused the symptoms in most of the attacks the boy had suffered.

A girl who was recently operated on had had a number of acute attacks, accompanied by high temperature, infection of the upper respiratory tract and considerable pus in the urine. She had been seen three times by a colleague and twice by one of my associates. I found considerable pus in the urine but could not find anything in the abdomen, and I told the parents I thought she did not have appendicitis. The family asked me to send the child to the hospital for roentgen examination. This was done and results of gastro-intestinal investigation with a barium meal were negative, but an enema showed a short broad appendix, and descending along this short appendix was a fine line of barium about 1½ inches (3.81 cm.) in length. Following the barium meal the child had more or less generalized abdominal pain which localized over McBurney's point, and we decided to explore the abdomen. At operation the proximal appendix, about 1 inch (2.54 cm.) in length, was broad but not inflamed; then came a complete kink in the appendix, and the last 1½ inches (3.81 cm.) were definitely inflamed. The roentgenologist had reported the results as negative.

Another case I have had occasion to follow through was that of a girl who was 3 years of age when I first saw her. She had an acute abdominal condition, and a history of having been operated on nine months before for intussusception. On that occasion a distinctly infiltrated appendix had been removed. When I saw the child she had the classic picture of intussusception, and on opening the abdomen we found an intussusception of the ileocecal valve, and the surgeon discovered a polyp in the intestine. That is the second case I have seen in which an operation was performed a second time for intussusception and a polyp found. This child did have an infiltrated appendix at the time of the first operation, but that was probably secondary to the interference with the circulation.

A word about pyuria and hematuria. We have recently had an interesting case in a girl, aged 16, who gave a history of having had repeated attacks of generalized abdominal pain. Her attending physician told her that because her pain was localized high up on the left that she was passing a renal calculus. We found microscopic blood in the urine and agreed with the diagnosis. The following day she developed pain in the right side, and roentgen examination revealed two small stones in the gallbladder which had no relationship to her present trouble. Due to a definite relationship between the time of her abdominal attacks and her menstrual periods, she was referred to a gynecologist who made a diagnosis and has since removed a large interligamentous cyst.

In another case the child remained well until about the age of 2, and then began having rather frequent attacks of abdominal cramps with periodic attacks of vomiting to the point of acidosis. After a diagnosis of probable duodenal stenosis this child finally came to operation, and the surgeon found a band about 2 inches (5.08 cm.) from the pylorus; this was removed, and the patient recovered.

I have detailed these cases because I have a definite feeling that in every case in which the condition is diagnosed as appendicitis, whether it is acute or

chronic, and in which there is not definite evidence to bear out the diagnosis at the time of operation, that further exploration should be made. I stress this because with a small muscle-splitting operation it may be necessary to enlarge the incision to make proper exploration.

DR. EDWIN M. MILLER: The paper was a clear discussion of the etiology, symptomatology, pathologic changes and, on the whole, the surgical treatment of the acute condition within the appendix in the child. I have come to the conclusion in my own work that acute appendicitis, whether in the child or the adult, is one of the most deciving things with which we have to deal, and the more experience I have in surgery the more uncertain I am as to my ability to make a diagnosis of appendicitis. When men of the caliber of Dr. Brennemann and Dr. Hess say that these cases present some of the most complex problems that may arise, I am sure that those statements are true. I believe that in every case in which there is a reasonable suspicion that one is dealing with an acute condition within the appendix, whether there is positive proof or not, the patient should be operated on.

I like to group these cases under three clinical heads: those in which the condition is obviously acute appendicitis, without rupture of the appendix; those which are obviously cases in which the appendix is ruptured, with more or less general involvement of the peritoneal cavity; and, third, those in which the appendix is definitely ruptured, with localized abscess formation. It seems to me that if the patient in the first group is seen early and is operated on promptly there should be no mortality. In the third group, when there is a definitely localized walled-off abscess, there should also be no mortality. The mortality should come only in the second group of cases, in which rupture has occurred with more or less involvement of the peritoneal cavity, without any tendency at all toward being walled off.

The treatment in these groups differs. I do not exactly agree with Dr. Portis that the patients in the group in which there is a definitely walled off appendiceal abscess should be operated on immediately. I think that is the type of case in which we should not be in any hurry about operating, and it is the only group in which I would not recommend immediate operation. I have found that we cannot always tell which way such an abscess is going to point, whether it will point toward the rectum and perhaps drain spontaneously, or whether it will come close to the abdominal wall in front and have to be opened through an abdominal incision. I see no necessity in such cases for making any serious attempt to remove the appendix, when it is not easily accessible and cannot be easily removed. We often find the pathologic process in the appendix limited to the tip, when it has ruptured, and a definitely walled off abscess has formed. In such a case not only would we be unable to find the entire appendix within that abscess but if we attempted to dig out that appendix, most of which lies without the abscess, we would endanger the life of the patient unnecessarily by opening up a clean peritoneal cavity, thus favoring the spread of the infection.

DR. KARL A. MEYER: The subject of acute appendicitis is to me the most interesting one in the entire domain of abdominal surgery.

Because of the comparatively high mortality it should be discussed frequently. The Chicago Pediatric Society is to be congratulated in choosing the subject for discussion this evening.

The mortality of acute cases still remains high. I would say, just as Dr. Portis showed, that in certain types of cases, the mortality reaches as high as 20 per cent. We find this in practice because we operate on patients who do not have appendicitis, but who have peritonitis.

The reason for the early development of peritonitis in children is obvious. The wall of the appendix is thin, and perforation ensues more rapidly than in the adult, hence the earlier rupture. The earlier the diagnosis is made and operation follows, the surer one can be of having an abdomen free from infection and a good result.

Dr. Brennemann's point about localized tenderness is true, not alone in the case of acute appendicitis, but in any inflammation in the abdominal cavity. Every

patient who has a syndrome of pain with localized tenderness and rigidity must be subjected to surgical intervention, if a low mortality is to be secured. In the after-care the mortality rate might be lowered by overcoming the dehydration that is present. Dr. Portis brought out this point with clearness.

In cases with beginning abscess it is a question whether intervention with operation should follow, or whether the mass be allowed to recede spontaneously or form a defined abscess. At this time simple drainage is all that is necessary.

In children with general peritonitis, one complication must always be looked for. When the temperature rises during convalescence following operation and the child suffers with rectal tenesmus with mucous discharge, a pelvic abscess should always be thought of. A rectal examination will help in making the diagnosis. When it points rectally, operation and drainage should be made through the anterior rectal wall. This will be found to be a life-saving measure.

DR. JESSE R. GERSTLEY: Would the essayist say a few words as to the value of x-ray pictures in recurrent appendicitis? In my own experience I have found them of no great help. I was interested in hearing Dr. Hess report that in one of his cases the roentgen examination did not confirm the diagnosis. I would be interested in Dr. Portis' views on the subject.

DR. I. MICHAEL LEVIN: It appears to me that the subject of acute appendicitis in children beyond the age of 5 or 6 years is much the same as in the adult. There is not sufficient emphasis on appendicitis in infants. It will be recalled that in 1917 Dr. Abt collected eighty cases from the literature in which the condition occurred in children under 2 years of ago.

During the last year I had occasion to operate on a male infant, aged 5½ months, who had no previous gastro-intestinal disturbance or infection of the upper respiratory tract, but had vomited several times and cried out in pain periodically. I saw him while he was asleep, and palpation of the right para-umbilical region resulted in pain and rigidity. The leukocyte count was 25,000; the urine was normal, and the temperature was 102 F. At operation I found an injected bulbous appendix which later, microscopically, showed early suppurative changes.

Since 1917, I have found forty-seven instances of appendicitis in the literature in children under 2 years of age, eighteen under 1 year and eight under 6 months. Hill and Mason, in 1925, reported a case of prenatal appendicitis with death occurring fifty-five hours after birth. Appendicitis in a hernial sac has been mentioned several times and should be borne in mind when children develop pain at the site of a hernia.

I have operated on a child, aged 8, with pin worms perforating the appendix. In another case a boy, aged 10, who had not experienced any abdominal pain, nausea, vomiting, or fever, complained of frequent urination of one week's duration. Pus was found in the urine, and, on careful examination of the abdomen, a large spherical, slightly tender mass seemed to project up from the pelvis. With a diagnosis of an infected cyst of the urachus, the abdomen was opened and an enormous appendiceal abscess was found, one wall of which was formed by the bladder. Death followed several operations for intestinal obstruction.

Of several points for emphasis, one is that the patient with an acute appendicitis is not a sick patient, while the child who is extremely ill probably has an infection of the upper respiratory tract with referred abdominal pain of toxic origin. An intelligent diagnosis should make early operative intervention possible within twenty-four hours of the onset.

DR. GEORGE E. BAXTER: I remember the first case of appendicitis that I saw in a child, aged 18 months, probably twenty years ago. At that time we did not make the diagnosis until the child had an acute condition within the appendix, and there were few cases reported in the literature in children under 2 years of age. I communicated with several men who had had larger experience than I, and several of them said there was no such thing as acute appendicitis in a child of that age.

I wish to stress one other condition, for we learn the most in the practice of medicine by our mistakes. I was called to see a patient with a good physician

who made a diagnosis of appendicitis, with which I agreed. The patient was sent to a hospital and seen by a surgeon, who also agreed. The leukocyte count was only 7,000 or 8,000, which caused them to hesitate, but still they operated. The appendix was normal, and the child was found to have typhoid fever, although there was a point of tenderness in the region of the appendix. I saw a similar case within the last year. The attending physician was not present when I examined the child, but I did not think the child had appendicitis. The physician, at my suggestion, removed the patient to the hospital for purpose of observation, but he called a surgeon, who thought it was appendicitis, and an operation was performed. There was no appendicitis, and that child had typhoid fever. Typhoid fever is not common, but neither is appendicitis as common as other forms of illness in children, but the fact that these two cases have occurred in my experience must mean that it is a point to consider in the differential diagnosis.

I wish to stress one other thing: we have cases of pyuria in children who have appendicitis. As Dr. Portis said, most of the patients are constipated, but some of them have diarrhea, and perhaps we are inclined to hide behind that idea and think the child has not an acute condition within the appendix. An experience within the last two months illustrates this point. I was called about 1 a. m. and told that a child was vomiting and had vomited five or six times. There was a history of diarrhea the day before while in school, and the mother had paid no attention to it. I assumed from that history that it was not an acute abdominal infection, but when I saw the child later in the morning I found evidence of peritonitis and of ruptured appendix. The cases of extreme and persistent vomiting which we see frequently in children, and abdominal pain which occurs from time to time, demand a careful abdominal examination. Some time we will find an acute condition within the appendix, and, of course, we do not wish to miss any of them.

I would hesitate to agree with Dr. Portis that in every case of infection of the upper respiratory tract accompanied by abdominal pain one is justified in performing an operation. I think we should be careful and make repeated examinations, for I do not think it is entirely without danger to subject a child with an infection of the upper respiratory tract to an abdominal operation.

Dr. A. H. Parmelee: I remember a case Dr. Hess also saw of a child who had acute abdominal pain, difficulty in urination and a distended bladder. Dr. Hess saw her just before going on his vacation, but had no opportunity to see her afterward. The child was sent to the hospital, and the following day developed complete paralysis of the lower extremities. The pain was originally in the right lower quadrant, excruciating in character, but there was a history of inability to urinate and pain in the bladder, which disappeared after catheterization. Then flaccid paralysis developed in both lower extremities. This was the first time I had seen this syndrome in the onset of a poliomyelitis.

Dr. Maurice L. Blatt: Differential diagnosis of several interesting abdominal conditions needs some comment.

While involvement of the urachus is not common, it does occur. There are two types: one intermittently opening into the urinary bladder and discharging its pus, the other closed at the lower end forming a large, midline, cystic tumor. A case falling in the first classification came under my observation several years ago; the condition cleared up promptly after drainage.

Pericarditis has to be differentiated from an acute appendicitis. Occasionally, it produces abdominal symptoms much as does pneumonia. Such a case was seen recently at Cook County Hospital; the condition was erroneously diagnosed as appendicitis, the appendix was removed and little evidence of a pathologic process was found. Typical pericardial symptoms occurred a few days later.

Abscess in the psoas muscle on the right side, whether due to tuberculosis or other cause, has to be thought of in differentiation. Prior to the use of x-rays a case of abscess of the psoas muscle came under my observation. It had the physical symptoms of an appendiceal abscess but no symptoms of peritoneal irritation. On operation a needle was found imbedded in an abscess in the psoas;

the appendix was normal. Perinephritic abscess when located on the right side produces symptoms simulating appendicitis. There is, however, pain and sometimes swelling in the lumbar region, high up. The symptoms of peritoneal irritation are usually absent.

DR. BERNARD PORTIS: I fully agree with Dr. Brennemann that localized tenderness is the most essential physical symptom; yet one must not forget that in the retrocecal location of the appendix this may be slight, and rectal examination may prove of great value. The leukocyte count is not entirely diagnostic as I have seen four patients with gangrenous appendicitis with normal counts; hence, I do not consider this symptom as definite indication for operation. The presence of red blood cells in the urine is frequently associated with ureteral irritation from the appendix, when it is retrocecal in position.

Dr. Hess has pointed to the frequent pain in the upper part of the abdomen. The majority of patients with acute and chronic appendicitis have pain in the part of the abdomen with great regularity, and this is dependent on spasm of the pylorus. The local tenderness over the appendix, however, usually points to it as the primary source of trouble.

I fully agree with Dr. Miller and Dr. Meyer in that one must be careful not to cause a generalized peritonitis when an abscess is encountered. My usual method is to remove the pus when an abscess is met with and gently try to find a line of cleavage to bring the appendix into the field. Sometimes the appendix is practically destroyed, but even here one must close over the communication with the cecum so as to prevent further fecal contamination of the peritoneal cavity and prevent the development of fecal fistula. I have not had a fecal fistula develop by following this method of management of the purulent and gangrenous appendixes. I cannot agree with Dr. Miller that the main pathologic process is located in the tip, as in many cases there are severe local changes in other parts of the appendix.

Replying to Dr. Gerstley, we have never used x-rays in the direct diagnosis of acute appendicitis, but this agent may be of help to differentiate renal calculi and pulmonary pathologic changes. In chronic appendicitis, the appendix usually remains filled for many days and is distinctly tender.

I agree with Dr. Levin that children with acute appendicitis are rarely markedly uncomfortable in the early stages, and some of the most severe conditions may not interfere with sleep.

Typhoid fever, mentioned by Dr. Baxter, should most certainly be considered especially in the presence of an epidemic. I did not make the statement that patients with infections of the upper respiratory tract and some symptoms simulating acute appendicitis should be operated on. I am definitely convinced, however, that in these patients who have abdominal symptoms which are definite for appendiceal involvement operation should be performed, and if necessary under a local anesthetic. I have yet to see any serious effects from the anesthetic of a few minutes' duration.

In any epidemic, and more especially influenza and infantile paralysis, one has to be extremely careful, as many bizzare abdominal pictures may be produced. Still if appendiceal involvement is seriously considered, it is far better to have the appendix out.

No matter what we may decide as to the form of therapy in a questionable case I do believe we must adhere to certain general rules. The patient must not be given any laxative, sedative or salicylate until the diagnosis of acute appendicitis has been ruled out. All of these patients should be put to bed and followed by careful observation of the abdominal symptoms and frequent leukocyte counts. I wish again to stress the need of cooperation of the surgeon and the pediatrician, as a diagnosis in these cases of acute appendicitis may be difficult and perplexing.

Book Reviews

Chirurgische Krankheiten im Kindesalter mit besonderer Berücksichtigung der einschlägigen Pädiatrischen Fragen. Erwin Gohrbandt, Paul Karger and Ernst Bergmann. Pp. 916. Berlin: S. Karger, 1928.

In this volume the authors aim to give the opinion of pediatrician and surgeon on subjects of interest to both, and this opinion is the result of agreement reached in consultation. The pediatric portion is written by Karger. A book like this will be welcome to many.

A future edition may strike a better balance by omitting too detailed description of surgical procedures, as for instance in the chapter on harelip and cleft palate. Here, the necessity of having the children in good nutritional condition, by tube feeding if necessary, and free from infections of the respiratory tract, could and should receive more attention. The amount of food given young infants is rather scanty, and advice to limit the amount of saline or Ringer's solution given parenterally in desiccated cases of toxicosis to small amounts seems somewhat strange.

The intraperitoneal administration of blood is not recommended for fear of adhesions. Every patient with scarlet fever is treated with serum. In serum treatments, precautions, when recommended, seem insufficient. In the chapter on erysipelas, roentgen therapy is omitted. The large doses of chloral hydrate given to infants had better be introduced by a smaller test dose whenever possible. The warning against opium and morphine in infancy might be modified and directed against the unnecessarily large doses which are often given. Description of the preparation for operation for exophthalmic goiter is deficient in omitting the preliminary treatment with sufficient doses of iodine. The simple thread method in treatment of strictures of the esophagus is not given. Transplantation of the ureters separately into the sigmoid in cases of extrophy of the bladder is not even mentioned. Nothing is said for or against the cutting of the sympathetic nerves in cases of cerebral palsy of childhood. The good results claimed in the treatment of bronchiectasis by limiting the fluid intake might be given better support.

The presentation of the treatment of status thymicolymphaticus, not only in its surgical aspects, is refreshingly sane. The warning not to separate the muscle fibers of the hypertrophic pylorus with the knife seems appropriate. When a patient with appendicitis is treated medically, great stress is laid on absolute immobilization of the intestines until localization is well established. The difficulty of diagnosis of appendicitis in childhood is fully recognized. The number of criticisms might be greater than those mentioned; at the same time, the many admirable features of the book greatly outweigh its shortcomings. Further editions, which no doubt will be in demand, will probably give better attention to American literature and include a chapter on the influence of heart disease in cases requiring surgical intervention.

Maternity and Child Welfare. Ethel Cassie. Price, 8 shillings and 6 pence. Pp. 288, with 13 illustrations and 3 plans. London: H. K. Lewis & Company, 1929.

This textbook has been written for the maternity and child welfare worker. The first fifty-five pages of the book are devoted to the administrative and general purpose of welfare and maternity care. The second section of the book deals with the essentials of infant feeding and child care. The last part concisely discusses the problems arising in the care of the ailing child. This should be an excellent book for nurses and for welfare workers, as the average publication is

either too elementary or too advanced to meet their requirements. The function of the worker in this field is the teaching of hygiene and the early detection and prevention of disease. This book gives a concise and readable discussion of these matters.

DIE AKUTE MITTELOHRENTZÜNDUNG ALS KINDERKRANKHEIT. A. FR. HECHT. Price, 7.80 marks. Pp. 126, with 17 charts and 6 tables. Berlin: Julius Springer, 1928.

The first nineteen pages of this book describe the anatomy, pathology and bacteriology of otitis media. The remaining pages are devoted to the frequency, course, symptoms, prognosis, and treatment of otitis media in the contagious diseases, nephritis and tuberculosis. It is excellently written, being concise, and the cases described are well chosen. The statistics given are from a sufficient number of cases to give them authority. This book should be of interest to the pediatrician as well as to the otologist.

DIE ERNÄHRUNG DES DIABETIKERS. By C. PIRQUET and R. WAGNER. Cloth. Pp. 182. Berlin: Urban & Schwarzenberg, 1928.

This book will be of little use to workers on this continent. The authors, after coining a few new words to make the "nem" system work in estimating diabetic diets, utilize about a third of the book to expatiate on the advantages and uses of this system in diabetes. The last two thirds of the book consists of recipes and tables of food values, which might have been useful had a more familiar terminology been used.

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CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. Thomas Crossan Clark, 51 Herkimer St., Hamilton, Ont.
Secretary-Treasurer: Dr. Frank H. Boone, 164 James St. S., Hamilton, Ont.

SECTIONAL

CENTRAL STATES PEDIATRIC SOCIETY

President: Dr. J. Gurney Taylor, 120 E. Wisconsin St., Milwaukee.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Ave., Chicago.
Place: Milwaukee. Time: October, 1929.

SECTION ON PEDIATRICS OF SOUTHERN MEDICAL ASSOCIATION

Chairman: Dr. J. H. Eugene Rosamond, 1074 Madison Ave., Memphis, Tenn.
Secretary: Dr. A. J. Waring, De Renne Apts., Savannah, Ga.
Place: Miami, Fla. Time: Nov. 20-22, 1929.

LOCAL

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. W. L. Channell, Medical Bldg., Oakland.
Secretary: Dr. J. E. Parrott, Medico-Dental Bldg., San Francisco.
Place: Various Teaching Schools. Time: Monthly.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. George P. Laton, 1136 W. 6th St., Los Angeles.
Secretary: Dr. William Sidney Bowers, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

THE ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Elsie Seelye Pratt, Republic Bldg., Denver.
Secretary and Treasurer: Dr. Wilford W. Barber, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month, 2:30 p. m., September to May, inclusive.

GEORGIA PEDIATRIC SOCIETY

President: Dr. W. N. Adkins, Medical Arts Bldg., Atlanta.
Secretary and Treasurer: Dr. E. N. Gleaton, 212 E. Gaston St., Savannah.

PEDIATRIC SECTION OF FULTON COUNTY MEDICAL SOCIETY, ATLANTA, GA.

Chairman: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Secretary: Dr. William Kiser, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St., Atlanta. Time: Second Thursday of each month from October to April, at 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Edwin T. Wyman, 483 Beacon St., Boston.
Secretary-Treasurer: Dr. Randolph K. Byers, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Maurice Blatt, 185 N. Wabash Ave., Chicago.
Secretary: Dr. J. K. Calvin, 104 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. L. R. De Buys, 1417 Delachaise St., New Orleans.
Secretary-Treasurer: Dr. C. T. Williams, 7401 Burthe St., New Orleans.

DETROIT PEDIATRIC SOCIETY

President: Dr. M. Boyd Kay, 10 Peterboro St., Detroit.
Secretary: Dr. Charles A. Wilson, 71 E. Ferry St., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. C. R. Moriarity, La Salle Bldg., Minneapolis.
Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Place: University Campus and Rochester, Minn. Time: Winter, Spring, Summer, Fall.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Park J. White, Beaumont Bldg., St. Louis.
Secretary-Treasurer: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

NEBRASKA-IOWA PEDIATRIC SOCIETY

President: Dr. Floyd Clarke, City Nat'l Bank Bldg., Omaha.
Secretary: Dr. R. B. Eldredge, Medical Arts Bldg., Omaha.
Place: Add-Sell Restaurant. Time: Second Thursday of each month from October to May, inclusive, 6 p. m.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Louis M. Ruderman, 961 Eastern Parkway, Brooklyn.
Secretary: Dr. Joseph F. Paulonis, 1357 Bushwick Ave., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

BRONX PEDIATRIC SOCIETY

President: Dr. William Hinz, 1964 Grand Concourse, New York.
Secretary: Dr. L. H. Barenberg, 1749 Grand Concourse, New York.
Place: Concourse Plaza, 161st St. and Grand Concourse, New York. Time: Second Wednesday of each month, except June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various Cities in New York. Time: Fourth Thursday of October, January and April.

PEDIATRIC SECTION OF THE NEW YORK ACADEMY OF MEDICINE

President: Dr. Stafford McLean, 17 E. 71st St., New York.
Secretary: Dr. F. Elmer Johnson, 300 West End Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. Paul W. Beaven, 26 S. Goodman St., Rochester, N. Y.
Secretary: Dr. Edwin R. Reynolds, 1620 St. Paul St., Rochester, N. Y.
Place: Arranged by Program Committee. Time: First Friday of each month from October to May.

THE PEDIATRIC SECTION OF THE ACADEMY OF MEDICINE OF CLEVELAND

Chairman: Dr. C. W. Wyckoff, 8314 Euclid Ave., Cleveland.
Secretary: Dr. C. L. Ruggles, 10616 Euclid Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22nd St., Philadelphia. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. Zaccheus R. Scott, Westinghouse Bldg., Pittsburgh.
Secretary: Dr. Theodore C. Elterich, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months.

THE SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. E. A. Hines, Seneca.
Secretary-Treasurer: Dr. R. M. Pollitzer, 105 E. North St., Greenville.
Place: Charleston. Time: May 8, 1929.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. A. G. Quinn, 1193 Madison Ave., Memphis, Tenn.
Secretary: Dr. Kinsey M. Buck, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

TEXAS PEDIATRIC SOCIETY

President: Dr. Edwin G. Schwarz, Medical Arts Bldg., Fort Worth.
Secretary-Treasurer: Dr. Ramsey Moore, Medical Arts Bldg., Dallas.

RICHMOND PEDIATRIC SOCIETY

President: Dr. J. B. Stone, 2042 Park Ave., Medical Arts Bldg., Richmond, Va.
Secretary: Dr. Samuel A. Anderson, Jr., 2326 W. Grace St. Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St., Richmond, Va. Time: First Thursday of each month (other than during the summer).

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Charles E. Conrad, Harrisonburg.
Secretary: Dr. William B. McIlwaine, Petersburg.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. E. D. Carder, 736 Granville St., Vancouver, B. C.
Secretary and Treasurer: Dr. George A. Lamont, 736 Granville St., Vancouver, B. C.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Arthur H. Gray, Lumber Exchange Bldg., Seattle.
Secretary: Dr. Armin Rembe, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, at 7 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. A. L. Kastner, 120 E. Wisconsin St., Milwaukee.
Secretary: Dr. F. R. Janney, 418 E. North Ave., Milwaukee.
Place: Children's Hospital, Milwaukee. Time: Second Wednesday of each alternate month, beginning with February.

PEDIATRIC SECTION, ACADEMY OF MEDICINE, TORONTO

Chairman: Dr. F. R. Hassard, 1361 King St. West, Toronto.
Secretary: Dr. G. A. Davis, 12 Belsize Dr., Toronto.
Time: November 17, December 15, February 16 and March 15.